Appendix A. Changes Between the Original and Current Comparative Effectiveness Review

The Key Questions (KQs) from the original comparative effectiveness review (CER) were reviewed by a stakeholder panel and underwent a public comment process via the AHRQ Effective Health Care Program website. There have been a few changes to the KQs. Rather than distinguishing between benefit outcomes primarily by type of outcome (symptom vs. other outcomes), they will be reported by timing and importance to patients; there is now only one KQ for benefits. Moreover, to enhance reporting on subgroups the previous KQ on subgroups has been integrated into the KQs on benefits and harms. The original CER used terminology specific to the Diagnostic and Statistical Manual of Mental Disorders – Fourth Edition (DSM-IV), and the conditions for this update have been revised according to changes in the DSM-V (e.g., pervasive developmental disorders is currently classified as an autism spectrum disorder) published in 2013.[1] None of these changes were anticipated to impact the categorization or inclusion of previous studies for this update. Diagnosis of study participants based on DSM-V was not mandatory for study inclusion. Specific changes are described below in terms of the PICOTS (population, intervention, comparators, outcomes, timing, and setting).

Population

In terms of the study population, there has been the (1) addition of depressive disorders, anxiety disorders, and substance use disorders; (2) broadening of anorexia nervosa to include other eating disorders, and of Tourette's syndrome to include all tic disorders; and (3) specification that the category of behavioral issues includes treatment of symptoms outside the context of a disorder, as for example when antipsychotics are prescribed for sedation/sleep within certain environmental contexts (e.g., residential facilities). While these latter uses of antipsychotics are not endorsed by guidelines or indicated for antipsychotic use as per FDA approval, it was thought important by our stakeholders to review the evidence on all current uses of antipsychotics to provide information of benefit and harms for a broad range of stakeholders. The subgroups have been modified slightly to include phase and features of disorder (e.g., acute vs. maintenance treatment), medication dose, and use for cases of refractory treatment; these reflect some major components of the uncertainty currently faced by many clinicians. We have indicated the difference between patient- and intervention-level characteristics (i.e., dose and co-interventions).

Interventions and Comparators

One long-standing FDA-approved FGA (molindone) was discontinued at the time of the original CER, but a generic has recently received approval for marketing and therefore this FGA has been added as an eligible antipsychotic. The SGA lurasidone was approved by the FDA in 2010 (for schizophrenia and later for bipolar depression, both in adults) and was not reviewed in the original CER. Two other SGAs were approved in 2015: brexpiprazole in July for schizophrenia and adjunctive treatment of major depression in adults, and cariprazine in September for schizophrenia and bipolar disorder in adults. The comparators remain the same: placebo/no treatment, same antipsychotic of different dose, and another antipsychotic.

Outcomes

There have been changes to the terminology and classification of some outcomes, for example removal of the wording "patient- or family-reported outcomes" from a single outcome, because several of the outcomes are measured by patient/family report. Despite changes, all of the previous included outcomes will be captured in some manner. There has been the addition of an outcome for global impressions, which captures symptoms and overall clinical improvement, severity, and functioning. The outcomes related to harms have been modified slightly to have better consistency with the categories of major and general adverse effects. The outcomes that will be graded for strength of evidence have been modified to be more precise for symptoms that are treated with antipsychotics for each condition (e.g., "autistic symptoms" has been replaced with irritability) and to reflect any changes to terminology and classification.

Timing and Setting

The same criteria will be used for timing (1987 or later) and setting (all settings). Outcomes will be categorized in terms of short- (<6 months) and long- (≥ 6 months-<12 months; 12 months+) term followup.

Study Design

The original inclusion criteria for study design have been broadened slightly to include additional forms of observational studies beyond comparative cohort studies; we included controlled before-and-after studies as well as pooled analysis of individual patient data from trials.

Methods

There were a few methodological changes to align the methods with current guidance of AHRQ's EPC program, and to potentially enhance our ability to inform decisions in some areas. The original assessment of SOE was frequently downgraded due to high risk of bias for the relevant studies, which included consideration of industry funding. Refinement in EPC program methods guidance on risk of bias assessments of individual studies, in particular in relation to the role of industry funding, may not lead to similar assessments in the updated review.[2] For some outcomes (especially harms which were evaluated across disorders), the use of mixed-comparison meta-analytical techniques (i.e., combining placebo and head-to-head trials across a variety of drug comparison) may be possible and allow for more quantitative assessment of differences between antipsychotics in the absence of many head-to-head trials. Moreover, the assessment of findings for patient and clinical subgroups relied upon within-study analyses which were highly variable and did not encompass harms data; applying analytical techniques with study-level data—although exploratory in nature[3]—would allow for examining the related key questions (KQ1a, b; KQ2 a, b) to a greater extent. Lastly, differences in some harms outcomes (e.g., weight gain and metabolic risks) have been shown to vary by condition,[4, 5] such that only using aggregate data on harms across conditions may not capture some information important for patient-level decision making. We attempted to differentiate the impact on harms within as well as across conditions.

References

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 5th ed. Washington, DC: American Psychiatric Association, 2013.

2. Viswanathan M, Ansari MT, Berkman ND, et al. Assessing the risk of bias of individual studies in systematic reviews of health care interventions methods guide for effectiveness and comparative effectiveness reviews. Rockville MD2008.

3. Higgins JPT, Green, S. Chapter 9: Analyzing data and undertaking meta-analysis. Cochrane Handbook for Systematic Reviews of Interventions: The Cochrane Collaboration; 2009.

4. De Hert M, Dobbelaere M, Sheridan EM, et al. Metabolic and endocrine adverse effects of second-generation antipsychotics in children and adolescents: A systematic review of randomized, placebo controlled trials and guidelines for clinical practice. Eur Psychiatry. 2011 Apr;26(3):144-58. PMID: 21295450.

5. Maayan L, Correll CU. Weight gain and metabolic risks associated with antipsychotic medications in children and adolescents. J Child Adolesc Psychopharmacol. 2011 Dec;21(6):517-35. PMID: 22166172.

Appendix B. Literature Search Strategies

Table B1. MEDLINE
Table B2. CENTRAL
Table B3. CINAHL
Table B4. Ovid EMBASE
Table B5. Ovid PsycINFO
Table B6. Dissertations and Theses International
Table B7. TOXLINE
Table B8. ClinicalTrials.gov
Table B9. WHO ICTRP

Table B1. MEDLINE

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present
Search Title: Antipsychotics_Child_Update
Search Date: 15 Oct 2015
Results: 6164

1. Adjustment Disorders/
2. Anorexia/
3. Anxiety/
4. exp Anxiety Disorders/
5. exp "Attention Deficit and Disruptive Behavior Disorders"/
6. exp Behavioral Symptoms/
7. Child Behavior Disorders/
8. exp Child Development Disorders, Pervasive/
9. exp Eating Disorders/
10. exp Hyperphagia/
11. exp Impulse Control Disorders/
12. exp Impulsive Behavior/
13. Irritable Mood/
14. Mental Disorders/
15. exp Mood Disorders/
16. Movement Disorders/
17. "Off-Label Use"/
18. Psychomotor Agitation/
19. Rett Syndrome/
20. exp "Schizophrenia and Disorders with Psychotic Features"/
21. Schizophrenia, Childhood/
22. exp Sleep Disorders/
23. exp Substance-Related Disorders/
24. exp Tic Disorders/
25. Violence/
26. (ADHD* or (attention deficit adj2 disorder*) or hyperkinetic syndrome).tw,kf.
27. ((adjustment or reactive) adj disorder*).tw,kf.
28. (affective adj2 (disorder* or disregulation or dysregulation)).tw,kf.
29. (aggressi* or agitat*).tw,kf.
30. agoraphobi*.tw,kf.
31. ((alcohol* or drug* or cannabi* or cocaine* or heroin or marijuana* or narcotic* or opiate* or opioid* or substance*) adj2 (abus* or addict* or depend* or disorder* or withdrawal*)).tw,kf.
32. ((addicti* or compulsi* or explosive or impuls*) adj2 (behavio* or disorder*)).tw,kf.
33. (((anankastic or compulsiv* or obsessive) adj (behavio* or disorder* or neuros* or personalit*)) or OCD).tw,kf.
34. anorexi*.tw,kf.
35. anxiety.tw,kf.
36. (autis* or asperger* or kanner* syndrome).tw,kf.
37. (behavio* adj2 (disorder* or disturb* or disrupt* or dyscontrol* or illness* or issue* or outburst* or problem*)).tw,kf.

38. (((behavio* or disorder* or episod*) adj (hypomanic or manic)) or mania*).tw,kf.
39. (binge adj (drink* or eat*)).tw,kf.
40. (bi polar or bipolar).tw,kf.
41. bulimi*.tw,kf.
42. (claustrophobi* or phobia* or phobic).tw,kf.
43. ((combat or war) adj (disorder* or neuros*)).tw,kf.
44. conduct disorder*.tw,kf.
45. cyclothymi*.tw,kf.
46. ((defiant or disrupt* or oppositional) adj (behavio* or disorder*)).tw,kf.
47. delusion*.tw,kf.
48. dementia praecox.tw,kf.
49. depress*.tw,kf.
50. ((dis integrative or disintegrative or dys integrative or dysintegrative) adj disorder*).tw,kf.
51. (dys somnia* or dyssomnia* or insomnia* or para somnia* or parasomnia*).tw,kf.
52. dysthymi*.tw,kf.
53. eating disorder*.tw,kf.
54. ((emotion* or mood) adj2 (disorder* or dis regulation or disregulation or dys regulation or dysregulation)).tw,kf.
55. (hoarder* or hoarding).tw,kf.
56. (hyper activ* or hyperactiv*).tw,kf.
57. hyperphagia*.tw,kf.
58. irritab*.tw,kf.
59. kleptomania*.tw,kf.
60. (minimal brain adj (dis function* or disfunction* or dys function* or dysfunction*)).tw,kf.
61. (mood adj2 (labil* or swing*)).tw,kf.
62. (off label* or offlabel* or unlabeled indication* or unlabeled use*).tw,kf.
63. (panic* adj (attack* or disorder*)).tw,kf.
64. (para suicid* or parasuicid*).tw,kf.
65. paranoi*.tw,kf.
66. pervasive development* disorder*.tw,kf.
67. ((post traumatic or posttraumatic) adj2 (disorder* or neuros*)).tw,kf.
68. ((psycho* or sociopath*) adj (disorder* or personalit*)).tw,kf.
69. psychos*.tw,kf.
70. PTSD*.tw,kf.
71. (rett* adj (syndrome* or disorder*)).tw,kf.
72. (self adj (destruct* or harm* or injur* or mutilat*)).tw,kf.
73. (schizo affect* or schizoaffect*).tw,kf.
74. schizophreni*.tw,kf.
75. shell shock*.tw,kf.
76. (sleep adj2 (disorder* or dysfunction*)).tw,kf.
77. stress disorder*.tw,kf.
78. tourette*.tw,kf.
79. tic disorder*.tw,kf.
80. unstable mood*.tw,kf.
81. violen*.tw,kf.
82. or/1-81

83. exp Antipsychotic Agents/
84. exp Butyrophenones/
85. exp Phenothiazines/
86. exp Thioxanthenes/
87. abilify.mp.
88. adasuve.mp.
89. aldazine.mp.
90. anatensol.mp.
91. anti naus.mp.
92. (anti psychotic* or antipsychotic*).mp.
93. aripiprazole.mp.
94. 82VFR53I78.rn.
95. arizole.mp.
96. asenapine.mp.
97. JKZ19V908O.rn.
98. atrolak.mp.
99. biquelle.mp.
100. brexpiprazole.mp.
101. 2J3YBM1K8C.rn.
102. buccastem.mp.
103. calmazine.mp.
104. cariprazine.mp.
105. chloractil.mp.
106. chlorpromanyl.mp.
107. chlorpromazine.mp.
108. U42B7VYA4P.rn.
109. clopine.mp.
110. clozapine.mp.
111. J60AR2IKIC.rn.
112. clozaril.mp.
113. compazine.mp.
114. compro.mp.
115. decazate.mp.
116. delucon.mp.
117. denzapine.mp.
118. dozic.mp.
119. droleptan.mp.
120. droperidol.mp.
121. O9U0F09D5X.rn.
122. ebesque.mp.
123. fanapt.mp.
124. fazaclo.mp.
125. fazalco.mp.
126. fentazin.mp.
127. fluphenazine.mp.
128. S79426A41Z.rn.

129. fortunan.mp.
130. geodon.mp.
131. haldol.mp.
132. halo peridol.mp.
133. haloperidol.mp.
134. J6292F8L3D.rn.
135. halperon.mp.
136. iloperidone.mp.
137. 133454-47-4.rn.
138. inapsine.mp.
139. invega.mp.
140. lanzek.mp.
141. largactil.mp.
142. latuda.mp.
143. loxapac.mp.
144. loxapine.mp.
145. LER583670J.rn.
146. loxitane.mp.
147. lurasidone.mp.
148. 22IC88528T.rn.
149. (major adj (tranquili?er* or tranquilli?er*)).mp.
150. mellaril*.mp.
151. melleril.mp.
152. mintreleq.mp.
153. moban.mp.
154. modecate.mp.
155. moditen.mp.
156. molindone.mp.
157. RT3Y3QMF8N.rn.
158. nausetil.mp.
159. navane.mp.
160. neuroleptic*.mp.
161. novo flurazine.mp.
162. novo peridol.mp.
163. novo ridazine.mp.
164. novo trifluzine.mp.
165. nu prochlor.mp.
166. olanzaccord.mp.
167. olanzapine.mp.
168. 132539-06-1.rn.
169. orap.mp.
170. ormazine.mp.
171. ozidal.mp.
172. ozin.mp.
173. paliperidone.mp.
174. 838F01T721.rn.

175. permitil.mp.
176. perphenazine.mp.
177. FTA7XXY4EZ.rn.
178. pimozide.mp.
179. 1HIZ4DL86F.rn.
180. procalm.mp.
181. prochlorazine.mp.
182. prochlorperazine.mp.
183. YHP6YLT61T.rn.
184. procomp.mp.
185. prolixin.mp.
186. promapar.mp.
187. prorazin.mp.
188. protran.mp.
189. proziere.mp.
190. prozine.mp.
191. quetiapine.mp.
192. BGL0JSY5SI.rn.
193. quetiaccord.mp.
194. quetin.mp.
195. resdone.mp.
196. rexulti.mp.
197. rideril.mp.
198. rispa.mp.
199. risperdal.mp.
200. risperidone.mp.
201. L6UH7ZF8HC.rn.
202. rispernia.mp.
203. rixadone.mp.
204. saphris.mp.
205. seotiapim.mp.
206. sequase.mp.
207. serenace.mp.
208. seronia.mp.
209. seroquel.mp.
210. solazine.mp.
211. sonazine.mp.
212. sondate.mp.
213. stelazine.mp.
214. stemetil.mp.
215. stemzine.mp.
216. sycrest.mp.
217. syquet.mp.
218. terfluzine.mp.
219. thioridazine.mp.
220. N3D6TG58NI.rn.

221. thiothixene.mp.
222. 7318FJ13YJ.rn.
223. thorazine.mp.
224. tiotixene.mp.
225. trifluoperazine.mp.
226. 214IZI85K3.rn.
227. trilafon.mp.
228. versacloz.mp.
229. vertigon.mp.
230. vraylar.mp.
231. xeplion.mp.
232. xomolix.mp.
233. xylac.mp.
234. zaluron.mp.
235. zaponex.mp.
236. zeldox.mp.
237. ziprasidone.mp.
238. 6UKA5VEJ6X.rn.
239. zylap.mp.
240. zypadhera.mp.
241. zypine.mp.
242. zyprexa.mp.
243. or/83-242
244. and/82,243
245. Adolescent/
246. Adolescent Medicine/
247. exp Child/
248. exp Minors/
249. exp Pediatrics/
250. exp Puberty/
251. Students/
252. Young Adult/
253. adolescen*.mp.
254. (boy* or girl* or teen*).mp.
255. (child* or grade school* or kid or kids or kindergar?en* or minors* or preschool* or pre school* or school age* or schoolchild* or toddler*).mp.
256. ((colleg* or high school* or highschool* or middle school* or universit*) adj2 (age* or student*)).mp.
257. (paediatric* or peadiatric* or pediatric*).mp.
258. (prepubescen* or pubescen* or pubert*).mp.
259. (young* adj (adult* or men or mens or people* or person* or women*)).mp.
260. (youth or youths).mp.
261. or/245-260
262. and/244,261
263. exp Epidemiologic Studies/
264. controlled clinical trial.pt.

265. randomized controlled trial.pt.
266. drug therapy.fs.
267. (case control or cohort* or follow up or followup or longitudinal or prospective* or retrospective).tw,kf.
268. ((compari* or epidemiologic* or experimental or observational) adj2 (analy* or study or studies)).tw,kf.
269. groups.ab.
270. placebo.ab.
271. random*.ab.
272. trial.ab.
273. or/263-272
274. exp animals/ not humans.sh.
275. 273 not 274
276. and/262,275
277. (case reports or comment or editorial or letter).pt.
278. 276 not 277
279. limit 278 to english
280. limit 279 to yr="1987-current"

Table B2. CENTRAL

Database: CENTRAL via Cochrane Library
Search Title: Antipsychotics_Child_Update
Date Searched: 19 Oct 2015
Results: 1569

1. [mh ^"Adjustment Disorders"]
2. [mh ^Anorexia]
3. [mh ^Anxiety]
4. [mh "Anxiety Disorders"]
5. [mh "Attention Deficit and Disruptive Behavior Disorders"]
6. [mh "Behavioral Symptoms"]
7. [mh ^"Child Behavior Disorders"]
8. [mh "Child Development Disorders, Pervasive"]
9. [mh "Eating Disorders"]
10. [mh Hyperphagia]
11. [mh "Impulse Control Disorders"]
12. [mh "Impulsive Behavior"]
13. [mh ^"Irritable Mood"]
14. [mh ^"Mental Disorders"]
15. [mh "Mood Disorders"]
16. [mh ^"Movement Disorders"]
17. [mh ^"Off-Label Use"]
18. [mh ^"Psychomotor Agitation"]
19. [mh ^"Rett Syndrome"]
20. [mh "Schizophrenia and Disorders with Psychotic Features"]
21. [mh ^"Schizophrenia, Childhood"]
22. [mh "Sleep Disorders"]

23. [mh "Substance-Related Disorders"]
24. [mh "Tic Disorders"]
25. [mh ^Violence]
26. (ADHD* or ("attention deficit" n/2 disorder*) or "hyperkinetic syndrome"):ti,ab,kw
27. ((adjustment or reactive) next disorder*):ti,ab,kw
28. (affective n/2 (disorder* or disregulation or dysregulation)):ti,ab,kw
29. (aggressi* or agitat*):ti,ab,kw
30. agoraphobi*:ti,ab,kw
31. ((alcohol* or drug* or cannabi* or cocaine* or heroin or marijuana* or narcotic* or opiate* or opioid* or substance*) n/2 (abus* or addict* or depend* or disorder* or withdrawal*)):ti,ab,kw
32. ((addicti* or compulsi* or explosive or impuls*) n/2 (behavio* or disorder*)):ti,ab,kw
33. (((anankastic or compulsiv* or obsessive) next (behavio* or disorder* or neuros* or personalit*)) or OCD):ti,ab,kw
34. anorexi*:ti,ab,kw
35. anxiety:ti,ab,kw
36. (autis* or asperger* or (kanner* next syndrome)):ti,ab,kw
37. (behavio* n/2 (disorder* or disturb* or disrupt* or dyscontrol* or illness* or issue* or outburst* or problem*)):ti,ab,kw
38. (((behavio* or disorder* or episod*) next (hypomanic or manic)) or mania*):ti,ab,kw
39. (binge next (drink* or eat*)):ti,ab,kw
40. ("bi polar" or bipolar):ti,ab,kw
41. bulimi*:ti,ab,kw
42. (claustrophobi* or phobia* or phobic):ti,ab,kw
43. ((combat or war) next (disorder* or neuros*)):ti,ab,kw
44. (conduct next disorder*):ti,ab,kw
45. cyclothymi*:ti,ab,kw
46. ((defiant or disrupt* or oppositional) next (behavio* or disorder*)):ti,ab,kw
47. delusion*:ti,ab,kw
48. "dementia praecox":ti,ab,kw
49. depress*:ti,ab,kw
50. (("dis integrative" or disintegrative or "dys integrative" or dysintegrative) next disorder*):ti,ab,kw
51. ((dys next somnia*) or dyssomnia* or insomnia* or (para next somnia*) or parasomnia*):ti,ab,kw
52. dysthymi*:ti,ab,kw
53. (eating next disorder*):ti,ab,kw
54. ((emotion* or mood) n/2 (disorder* or "dis regulation" or disregulation or "dys regulation" or dysregulation)):ti,ab,kw
55. (hoarder* or hoarding):ti,ab,kw
56. ((hyper next activ*) or hyperactiv*):ti,ab,kw
57. (hyperphagia*):ti,ab,kw
58. (irritab*):ti,ab,kw
59. (kleptomania*):ti,ab,kw
60. ("minimal brain" next ((dis next function*) or disfunction* or (dys next function*) or dysfunction*)):ti,ab,kw

61. (mood n/2 (labil* or swing*)):ti,ab,kw
62. ((off next label*) or offlabel* or (unlabeled next indication*) or (unlabeled next use*)):ti,ab,kw
63. (panic* next (attack* or disorder*)):ti,ab,kw
64. ((para next suicid*) or parasuicid*):ti,ab,kw
65. (paranoi*):ti,ab,kw
66. (pervasive next development* next disorder*):ti,ab,kw
67. (("post traumatic" or posttraumatic) n/2 (disorder* or neuros*)):ti,ab,kw
68. ((psycho* or sociopath*) next (disorder* or personalit*)):ti,ab,kw
69. (psychos*):ti,ab,kw
70. (PTSD*):ti,ab,kw
71. (rett* next (syndrome* or disorder*)):ti,ab,kw
72. (self next (destruct* or harm* or injur* or mutilat*)):ti,ab,kw
73. ((schizo next affect*) or schizoaffect*):ti,ab,kw
74. (schizophreni*):ti,ab,kw
75. (shell next shock*):ti,ab,kw
76. (sleep n/2 (disorder* or dysfunction*)):ti,ab,kw
77. (stress next disorder*):ti,ab,kw
78. (tourette*):ti,ab,kw
79. (tic next disorder*):ti,ab,kw
80. (unstable next mood*):ti,ab,kw
81. violen*:ti,ab,kw
82. {or #1-#81}
83. [mh "Antipsychotic Agents"]
84. [mh Butyrophenones]
85. [mh Phenothiazines]
86. [mh Thioxanthenes]
87. (abilify or adasuve or aldazine or anatensol or "anti naus"):ti,ab,kw
88. ((anti next psychotic*) or antipsychotic*):ti,ab,kw
89. (aripiprazole or arizole or asenapine or atrolak or biquelle):ti,ab,kw
90. (brexpiprazole or buccastem or calmazine or cariprazine or chloractil):ti,ab,kw
91. (chlorpromanyl or chlorpromazine or clopine or clozapine or clozaril):ti,ab,kw
92. (compazine or compro or decazate or delucon or denzapine):ti,ab,kw
93. (dozic or droleptan or droperidol or ebesque or fanapt):ti,ab,kw
94. (fazaclo or fazalco or fentazin or fluphenazine or fortunan):ti,ab,kw
95. (geodon or haldol or "halo peridol" or haloperidol or halperon):ti,ab,kw
96. (iloperidone or inapsine or invega or lanzek or largactil):ti,ab,kw
97. (latuda or loxapac or loxapine or loxitane or lurasidone):ti,ab,kw
98. (major next (tranquili?er* or tranquilli?er*)):ti,ab,kw
99. (mellaril* or melleril or mintreleq or moban or modecate):ti,ab,kw
100. (moditen or molindone or nausetil or navane):ti,ab,kw
101. (neuroleptic*):ti,ab,kw
102. ("novo flurazine" or "novo peridol" or "novo ridazine" or "novo trifluzine" or "nu prochlor"):ti,ab,kw
103. (olanzaccord or olanzapine or orap or ormazine or ozidal):ti,ab,kw
104. (ozin or paliperidone or permitil or perphenazine or pimozide):ti,ab,kw

105. (procalm or prochlorazine or prochlorperazine or procomp or prolixin):ti,ab,kw
106. (promapar or prorazin or protran or proziere or prozine):ti,ab,kw
107. (quetiapine or quetiaccord or quetin or resdone or rexulti):ti,ab,kw
108. (rideril or rispa or risperdal or risperidone or rispernia):ti,ab,kw
109. (rixadone or saphris or seotiapim or sequase or serenace):ti,ab,kw
110. (seronia or seroquel or solazine or sonazine or sondate):ti,ab,kw
111. (stelazine or stemetil or stemzine or sycrest or syquet):ti,ab,kw
112. (terfluzine or thioridazine or thiothixene or thorazine or tiotixene):ti,ab,kw
113. (trifluoperazine or trilafon or versacloz or vertigon or vraylar):ti,ab,kw
114. (xeplion or xomolix or xylac or zaluron or zaponex):ti,ab,kw
115. (zeldox or ziprasidone or zylap or zypadhera or zypine or zyprexa):ti,ab,kw
116. {or #83-#115}
117. #82 and #116
118. [mh ^Adolescent]
119. [mh ^"Adolescent Medicine"]
120. [mh Child]
121. [mh Minors]
122. [mh Pediatrics]
123. [mh Puberty]
124. [mh ^Students]
125. [mh ^"Young Adult"]
126. (adolescen*):ti,ab,kw
127. (boy* or girl* or teen*):ti,ab,kw
128. (child* or (grade next school*) or kid or kids or kindergar?en* or minors* or preschool* or (pre next school*) or (school next age*) or schoolchild* or toddler*):ti,ab,kw
129. ((colleg* or (high next school*) or highschool* or (middle next school*) or universit*) n/2 (age* or student*)):ti,ab,kw
130. (paediatric* or peadiatric* or pediatric*):ti,ab,kw
131. (prepubescen* or pubescen* or pubert*):ti,ab,kw
132. (young* next (adult* or men or mens or people* or person* or women*)):ti,ab,kw
133. (youth or youths):ti,ab,kw
134. {or #118-#133}
135. #117 and #134 Publication Year from 1987 to 2015, in Trials

Note: Excluded 73 non-English language records in EndNote

Table B3. CINAHL

Database: CINAHL Plus with Full Text via EbscoHOST
Search Title: Antipsychotics_Child_Update
Date Searched: 21 Oct 2015
Results: 1142

S1. MH "Adjustment Disorders+"
S2. MH "Affective Disorders+"
S3. MH "Affective Disorders, Psychotic+"
S4. MH "Affective Symptoms+"
S5. MH "Anxiety Disorders+"

S6. MH "Attention Deficit Hyperactivity Disorder"
S7. MH "Behavior, Addictive+"
S8. MH "Behavioral Symptoms"
S9. MH "Child Behavior Disorders"
S10. MH "Child Development Disorders, Pervasive+"
S11. MH "Compulsive Behavior"
S12. MH "Drugs, Off-Label"
S13. MH "Eating Disorders+"
S14. MH "Impulse Control Disorders+"
S15. MH "Mental Disorders"
S16. MH "Mental Disorders Diagnosed in Childhood"
S17. MH "Paranoid Disorders"
S18. MH "Psychomotor Agitation"
S19. MH "Psychomotor Disorders"
S20. MH "Psychotic Disorders+"
S21. MH "Rett Syndrome"
S22. MH "Schizoaffective Disorder"
S23. MH "Schizophrenia+"
S24. MH "Sleep Disorders+"
S25. MH "Substance Use Disorders+"
S26. MH "Suicide+"
S27. MH "Tourette Syndrome"
S28. MH "Violence"
S29. (ADHD* or ("attention deficit" N2 disorder*) or "hyperkinetic syndrome")
S30. ((adjustment or reactive) N1 disorder*)
S31. (affective N2 (disorder* or disregulation or dysregulation))
S32. (aggressi* or agitat*)
S33. agoraphobi*
S34. ((alcohol* or drug* or cannabi* or cocaine* or heroin or marijuana* or narcotic* or opiate* or opioid* or substance*) N2 (abus* or addict* or depend* or disorder* or withdrawal*))
S35. ((addicti* or compulsi* or explosive or impuls*) N2 (behavio* or disorder*))
S36. (((anankastic or compulsiv* or obsessive) N1 (behavio* or disorder* or neuros* or personalit*)) or OCD)
S37. anorexi*
S38. anxiety
S39. (autis* or asperger* or "kanner* syndrome")
S40. (behavio* N2 (disorder* or disturb* or disrupt* or dyscontrol* or illness* or issue* or outburst* or problem*))
S41. (((behavio* or disorder* or episod*) N1 (hypomanic or manic)) or mania*)
S42. (binge N1 (drink* or eat*))
S43. ("bi polar" or bipolar)
S44. bulimi*
S45. (claustrophobi* or phobia* or phobic)
S46. ((combat or war) N1 (disorder* or neuros*))
S47. "conduct disorder*"
S48. cyclothymi*

S49. ((defiant or disrupt* or oppositional) N1 (behavio* or disorder*))
S50. delusion*
S51. "dementia praecox"
S52. depress*
S53. (("dis integrative" or disintegrative or "dys integrative" or dysintegrative) N1 disorder*)
S54. ("dys somnia*" or dyssomnia* or insomnia* or "para somnia*" or parasomnia*)
S55. dysthymi*
S56. "eating disorder*"
S57. ((emotion* or mood) N2 (disorder* or "dis regulation" or disregulation or "dys regulation" or dysregulation))
S58. (hoarder* or hoarding)
S59. ("hyper activ*" or hyperactiv*)
S60. hyperphagia*
S61. irritab*
S62. kleptomania*
S63. ("minimal brain" N1 ("dis function*" or disfunction* or "dys function*" or dysfunction*))
S64. (mood N2 (labil* or swing*))
S65. ("off label*" or offlabel* or "unlabeled indication*" or "unlabeled use*")
S66. (panic* N1 (attack* or disorder*))
S67. ("para suicid*" or parasuicid*)
S68. paranoi*
S69. "pervasive development* disorder*"
S70. (("post traumatic" or posttraumatic) N2 (disorder* or neuros*))
S71. ((psycho* or sociopath*) N1 (disorder* or personalit*))
S72. psychos*
S73. PTSD*
S74. (rett* N1 (syndrome* or disorder*))
S75. (self N1 (destruct* or harm* or injur* or mutilat*))
S76. ("schizo affect*" or schizoaffect*)
S77. schizophreni*
S78. "shell shock*"
S79. (sleep N2 (disorder* or dysfunction*))
S80. "stress disorder*"
S81. tourette*
S82. "tic disorder*"
S83. "unstable mood*"
S84. violen*
S85. S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54 OR S55 OR S56 OR S57 OR S58 OR S59 OR S60 OR S61 OR S62 OR S63 OR S64 OR S65 OR S66 OR S67 OR S68 OR S69 OR S70 OR S71 OR S72 OR S73 OR S74 OR S75 OR S76 OR S77 OR S78 OR S79 OR S80 OR S81 OR S82 OR S83 OR S84
S86. MH "Antipsychotic Agents+"

S87. (abilify or adasuve or aldazine or anatensol or "anti naus")
S88. ("anti psychotic*" or antipsychotic*)
S89. (aripiprazole or arizole or asenapine or atrolak or biquelle)
S90. (brexpiprazole or buccastem or calmazine or cariprazine or chloractil)
S91. (chlorpromanyl or chlorpromazine or clopine or clozapine or clozaril)
S92. (compazine or compro or decazate or delucon or denzapine)
S93. (dozic or droleptan or droperidol or ebesque or fanapt)
S94. (fazaclo or fazalco or fentazin or fluphenazine or fortunan)
S95. (geodon or haldol or "halo peridol" or haloperidol or halperon)
S96. (iloperidone or inapsine or invega or lanzek or largactil)
S97. (latuda or loxapac or loxapine or loxitane or lurasidone)
S98. (major N1 (tranquili?er* or tranquilli?er*))
S99. (mellaril* or melleril or mintreleq or moban or modecate)
S100. (moditen or molindone or nausetil or navane)
S101. neuroleptic*
S102. (novo N1 (flurazine or peridol or ridazine or trifluzine))
S103. ("nu prochlor" or olanzaccord or olanzapine or orap or ormazine)
S104. (ozidal or ozin or paliperidone or permitil or perphenazine)
S105. (pimozide or procalm or prochlorazine or prochlorperazine or procomp)
S106. (prolixin or promapar or prorazin or protran or proziere)
S107. (prozine or quetiapine or quetiaccord or quetin or resdone)
S108. (rexulti or rideril or rispa or risperdal or risperidone)
S109. (rispernia or rixadone or saphris or seotiapim or sequase)
S110. (serenace or seronia or seroquel or solazine or sonazine)
S111. (sondate or stelazine or stemetil or stemzine or sycrest)
S112. (syquet or terfluzine or thioridazine or thiothixene or thorazine)
S113. (tiotixene or trifluoperazine or trilafon or versacloz or vertigon)
S114. (vraylar or xeplion or xomolix or xylac or zaluron)
S115. (zaponex or zeldox or ziprasidone or zylap or zypadhera)
S116. (zypine or zyprexa)
S117. S86 OR S87 OR S88 OR S89 OR S90 OR S91 OR S92 OR S93 OR S94 OR S95 OR S96 OR S97 OR S98 OR S99 OR S100 OR S101 OR S102 OR S103 OR S104 OR S105 OR S106 OR S107 OR S108 OR S109 OR S110 OR S111 OR S112 OR S113 OR S114 OR S115 OR S116
S118. S85 AND S117
S119. MH "Adolescence+"
S120. MH "Adolescent Medicine"
S121. MH "Child"
S122. MH "Child, Preschool"
S123. MH "Minors (Legal)"
S124. MH "Pediatrics"
S125. MH "Puberty"
S126. MH "Students, Elementary"
S127. MH "Students, High School"
S128. MH "Students, Middle School"
S129. MH "Students, Undergraduate"

S130. MH "Young Adult"
S131. adolescen*
S132. (boy* or girl* or teen*)
S133. (child* or "grade school*" or kid or kids or kindergar?en* or minors* or preschool* or "pre school*" or "school age*" or schoolchild* or toddler*)
S134. ((colleg* or "high school*" or highschool* or "middle school*" or universit*) N2 (age* or student*))
S135. (paediatric* or peadiatric* or pediatric*)
S136. (prepubescen* or pubescen* or pubert*)
S137. (young* N1 (adult* or men or mens or people* or person* or women*))
S138. (youth or youths)
S139. S119 OR S120 OR S121 OR S122 OR S123 OR S124 OR S125 OR S126 OR S127 OR S128 OR S129 OR S130 OR S131 OR S132 OR S133 OR S134 OR S135 OR S136 OR S137 OR S138
S140. S118 AND S139
S141. MH "Clinical Research+"
S142. MH "Comparative Studies"
S143. MH "Drug Therapy"
S144. MH "Experimental Studies+"
S145. MH "Nonexperimental Studies+"
S146. MH "Retrospective Design"
S147. Limiters - Publication Type: Clinical Trial, Randomized Controlled Trial
S148. ("case control" or cohort* or "follow up" or followup or longitudinal or prospective* or retrospective)
S149. ((compari* or epidemiologic* or experimental or observational) N2 (analy* or study or studies))
S150. AB groups
S151. AB placebo
S152. AB random*
S153. AB trial
S154. S141 OR S142 OR S143 OR S144 OR S145 OR S146 OR S147 OR S148 OR S149 OR S150 OR S151 OR S152 OR S153
S155. (MH "Animals+") not (MH "Humans")
S156. S154 NOT S155
S157. S140 AND S156
S158. PT (“case reports” or comment or editorial or letter)
S159. S157 NOT S158
S160. S159 Limiters – Language: English
S161. S160 Limiters – English Language; Published Date: 19870101-20151231

Table B4. Ovid EMBASE

Database: Ovid Embase 1980 to 2015 Week 41
Search Title: Antipsychotics_Child_Update_1
Date Searched: 16 Oct 2015
Results: 7376

1. abnormal behavior/

2. exp addiction/
3. adjustment disorder/
4. aggression/
5. aggressiveness/
6. exp anger/
7. anorexia/
8. anxiety/
9. exp anxiety disorder/
10. attention deficit disorder/
11. exp autism/
12. automutilation/
13. behavior disorder/
14. disruptive behavior/
15. exp eating disorder/
16. exp impulse control disorder/
17. impulsiveness/
18. intermittent explosive disorder/
19. irritability/
20. kleptomania/
21. oppositional defiant disorder/
22. exp psychosis/
23. exp psychosocial disorder/
24. exp "substance use"/
25. exp suicidal behavior/
26. mental disease/
27. minimal brain dysfunction/
28. exp mood disorder/
29. motor dysfunction/
30. "off label drug use"/
31. restlessness/
32. exp sleep disorder/
33. exp tic/
34. exp violence/
35. (ADHD* or (attention deficit adj2 disorder*) or hyperkinetic syndrome).tw.
36. ((adjustment or reactive) adj disorder*).tw.
37. (affective adj2 (disorder* or disregulation or dysregulation)).tw.
38. (aggressi* or agitat*).tw.
39. agoraphobi*.tw.
40. ((alcohol* or drug* or cannabi* or cocaine* or heroin or marijuana* or narcotic* or opiate* or opioid* or substance*) adj2 (abus* or addict* or depend* or disorder* or withdrawal*)).tw.
41. ((addicti* or compulsi* or explosive or impuls*) adj2 (behavio* or disorder*)).tw.
42. (((anankastic or compulsiv* or obsessive) adj (behavio* or disorder* or neuros* or personalit*)) or OCD).tw.
43. anorexi*.tw.
44. anxiety.tw.
45. (autis* or asperger* or kanner* syndrome).tw.

46. (behavio* adj2 (disorder* or disturb* or disrupt* or dyscontrol* or illness* or issue* or outburst* or problem*)).tw.
47. (((behavio* or disorder* or episod*) adj (hypomanic or manic)) or mania*).tw.
48. (binge adj (drink* or eat*)).tw.
49. (bi polar or bipolar).tw.
50. bulimi*.tw.
51. (claustrophobi* or phobia* or phobic).tw.
52. ((combat or war) adj (disorder* or neuros*)).tw.
53. conduct disorder*.tw.
54. cyclothymi*.tw.
55. ((defiant or disrupt* or oppositional) adj (behavio* or disorder*)).tw.
56. delusion*.tw.
57. dementia praecox.tw.
58. depress*.tw.
59. ((dis integrative or disintegrative or dys integrative or dysintegrative) adj disorder*).tw.
60. (dys somnia* or dyssomnia* or insomnia* or para somnia* or parasomnia*).tw.
61. dysthymi*.tw.
62. eating disorder*.tw.
63. ((emotion* or mood) adj2 (disorder* or dis regulation or disregulation or dys regulation or dysregulation)).tw.
64. (hoarder* or hoarding).tw.
65. (hyper activ* or hyperactiv*).tw.
66. hyperphagia*.tw.
67. irritab*.tw.
68. kleptomania*.tw.
69. (minimal brain adj (dis function* or disfunction* or dys function* or dysfunction*)).tw.
70. (mood adj2 (labil* or swing*)).tw.
71. (off label* or offlabel* or unlabeled indication* or unlabeled use*).tw.
72. (panic* adj (attack* or disorder*)).tw.
73. (para suicid* or parasuicid*).tw.
74. paranoi*.tw.
75. pervasive development* disorder*.tw.
76. ((post traumatic or posttraumatic) adj2 (disorder* or neuros*)).tw.
77. ((psycho* or sociopath*) adj (disorder* or personalit*)).tw.
78. psychos*.tw.
79. PTSD*.tw.
80. (rett* adj (syndrome* or disorder*)).tw.
81. (self adj (destruct* or harm* or injur* or mutilat*)).tw.
82. (schizo affect* or schizoaffect*).tw.
83. schizophreni*.tw.
84. shell shock*.tw.
85. (sleep adj2 (disorder* or dysfunction*)).tw.
86. stress disorder*.tw.
87. tourette*.tw.
88. tic disorder*.tw.
89. unstable mood*.tw.

90. violen*.tw.
91. or/1-90
92. abilify.mp.
93. adasuve.mp.
94. aldazine.mp.
95. anatensol.mp.
96. anti naus.mp.
97. (anti psychotic* or antipsychotic*).tw.
98. aripiprazole.mp.
99. arizole.mp.
100. asenapine.mp.
101. atrolak.mp.
102. biquelle.mp.
103. brexpiprazole.mp.
104. buccastem.mp.
105. calmazine.mp.
106. cariprazine.mp.
107. chloractil.mp.
108. chlorpromanyl.mp.
109. chlorpromazine.mp.
110. clopine.mp.
111. clozapine.mp.
112. clozaril.mp.
113. compazine.mp.
114. compro.mp.
115. decazate.mp.
116. delucon.mp.
117. denzapine.mp.
118. dozic.mp.
119. droleptan.mp.
120. droperidol.mp.
121. ebesque.mp.
122. fanapt.mp.
123. fazaclo.mp.
124. fazalco.mp.
125. fentazin.mp.
126. fluphenazine.mp.
127. fortunan.mp.
128. geodon.mp.
129. haldol.mp.
130. halo peridol.mp.
131. haloperidol.mp.
132. halperon.mp.
133. iloperidone.mp.
134. inapsine.mp.
135. invega.mp.

136. lanzek.mp.
137. largactil.mp.
138. latuda.mp.
139. loxapac.mp.
140. loxapine.mp.
141. loxitane.mp.
142. lurasidone.mp.
143. (major adj (tranquili?er* or tranquilli?er*)).tw.
144. mellaril*.mp.
145. melleril.mp.
146. mintreleq.mp.
147. moban.mp.
148. modecate.mp.
149. moditen.mp.
150. molindone.mp.
151. nausetil.mp.
152. navane.mp.
153. neuroleptic*.tw.
154. novo flurazine.mp.
155. novo peridol.mp.
156. novo ridazine.mp.
157. novo trifluzine.mp.
158. nu prochlor.mp.
159. olanzaccord.mp.
160. olanzapine.mp.
161. orap.mp.
162. ormazine.mp.
163. ozidal.mp.
164. ozin.mp.
165. paliperidone.mp.
166. permitil.mp.
167. perphenazine.mp.
168. pimozide.mp.
169. procalm.mp.
170. prochlorazine.mp.
171. prochlorperazine.mp.
172. procomp.mp.
173. prolixin.mp.
174. promapar.mp.
175. prorazin.mp.
176. protran.mp.
177. proziere.mp.
178. prozine.mp.
179. quetiapine.mp.
180. quetiaccord.mp.
181. quetin.mp.

182. resdone.mp.
183. rexulti.mp.
184. rideril.mp.
185. rispa.mp.
186. risperdal.mp.
187. risperidone.mp.
188. rispernia.mp.
189. rixadone.mp.
190. saphris.mp.
191. seotiapim.mp.
192. sequase.mp.
193. serenace.mp.
194. seronia.mp.
195. seroquel.mp.
196. solazine.mp.
197. sonazine.mp.
198. sondate.mp.
199. stelazine.mp.
200. stemetil.mp.
201. stemzine.mp.
202. sycrest.mp.
203. syquet.mp.
204. terfluzine.mp.
205. thioridazine.mp.
206. thiothixene.mp.
207. thorazine.mp.
208. tiotixene.mp.
209. trifluoperazine.mp.
210. trilafon.mp.
211. versacloz.mp.
212. vertigon.mp.
213. vraylar.mp.
214. xeplion.mp.
215. xomolix.mp.
216. xylac.mp.
217. zaluron.mp.
218. zaponex.mp.
219. zeldox.mp.
220. ziprasidone.mp.
221. zylap.mp.
222. zypadhera.mp.
223. zypine.mp.
224. zyprexa.mp.
225. or/92-224
226. and/91,225
227. adolescen*.mp.

228. (boy* or girl* or teen*).mp.
229. (child* or grade school* or kid or kids or kindergar?en* or minors* or preschool* or pre school* or school age* or schoolchild* or toddler*).mp.
230. (paediatric* or peadiatric* or pediatric*).mp.
231. (prepubescen* or pubescen* or pubert*).mp.
232. (young* adj (adult* or men or mens or people* or person* or women*)).mp.
233. (youth or youths).mp.
234. or/227-233
235. and/226,234
236. exp comparative study/
237. exp controlled study/
238. experimental study/
239. observational study/
240. dt.fs.
241. (case control or cohort* or follow up or followup or longitudinal or prospective* or retrospective).tw.
242. ((compari* or epidemiologic* or experimental or observational) adj2 (analy* or study or studies)).tw.
243. groups.ab.
244. placebo.ab.
245. random*.ab.
246. trial.ab.
247. or/236-246
248. animals/ not (animals/ and humans/)
249. 247 not 248
250. and/235,249
251. (conference* or editorial or letter).pt.
252. 250 not 251
253. limit 252 to english
254. limit 253 to yr="1987-current"

Table B5. Ovid PsycINFO

Database: Ovid PsycINFO 1987 to October Week 2 2015
Search Title: Antipsychotics_Child_Update_2
Date Searched: 20 Oct 2015
Results: 2296

1. Adjustment Disorders/
2. exp Affective Disorders/
3. Aggressive Behavior/
4. Agitation/
5. Anxiety/
6. exp Anxiety Disorders/
7. exp Attention Deficit Disorder/
8. exp Behavior Disorders/
9. exp Behavior Problems/
10. Conduct Disorder/

11. exp Drug Usage/
12. exp Eating Disorders/
13. exp Impulse Control Disorders/
14. Impulsiveness/
15. Irritability/
16. Kleptomania/
17. Mental Disorders/
18. Movement Disorders/
19. Oppositional Defiant Disorder/
20. exp Pervasive Developmental Disorders/
21. Psychiatric Patients/
22. Psychiatric Symptoms/
23. exp Psychosis/
24. Schizoaffective Disorder/
25. exp Sleep Disorders/
26. Tics/
27. Tourette Syndrome/
28. Violence/
29. (ADHD* or (attention deficit adj2 disorder*) or hyperkinetic syndrome).tw.
30. ((adjustment or reactive) adj disorder*).tw.
31. (affective adj2 (disorder* or disregulation or dysregulation)).tw.
32. (aggressi* or agitat*).tw.
33. agoraphobi*.tw.
34. ((alcohol* or drug* or cannabi* or cocaine* or heroin or marijuana* or narcotic* or opiate* or opioid* or substance*) adj2 (abus* or addict* or depend* or disorder* or withdrawal*)).tw.
35. ((addicti* or compulsi* or explosive or impuls*) adj2 (behavio* or disorder*)).tw.
36. (((anankastic or compulsiv* or obsessive) adj (behavio* or disorder* or neuros* or personalit*)) or OCD).tw.
37. anorexi*.tw.
38. anxiety.tw.
39. (autis* or asperger* or kanner* syndrome).tw.
40. (behavio* adj2 (disorder* or disturb* or disrupt* or dyscontrol* or illness* or issue* or outburst* or problem*)).tw.
41. (((behavio* or disorder* or episod*) adj (hypomanic or manic)) or mania*).tw.
42. (binge adj (drink* or eat*)).tw.
43. (bi polar or bipolar).tw.
44. bulimi*.tw.
45. (claustrophobi* or phobia* or phobic).tw.
46. ((combat or war) adj (disorder* or neuros*)).tw.
47. conduct disorder*.tw.
48. cyclothymi*.tw.
49. ((defiant or disrupt* or oppositional) adj (behavio* or disorder*)).tw.
50. delusion*.tw.
51. dementia praecox.tw.
52. depress*.tw.
53. ((dis integrative or disintegrative or dys integrative or dysintegrative) adj disorder*).tw.

54. (dys somnia* or dyssomnia* or insomnia* or para somnia* or parasomnia*).tw.
55. dysthymi*.tw.
56. eating disorder*.tw.
57. ((emotion* or mood) adj2 (disorder* or dis regulation or disregulation or dys regulation or dysregulation)).tw.
58. (hoarder* or hoarding).tw.
59. (hyper activ* or hyperactiv*).tw.
60. hyperphagia*.tw.
61. irritab*.tw.
62. kleptomania*.tw.
63. (minimal brain adj (dis function* or disfunction* or dys function* or dysfunction*)).tw.
64. (mood adj2 (labil* or swing*)).tw.
65. (off label* or offlabel* or unlabeled indication* or unlabeled use*).tw.
66. (panic* adj (attack* or disorder*)).tw.
67. (para suicid* or parasuicid*).tw.
68. paranoi*.tw.
69. pervasive development* disorder*.tw.
70. ((post traumatic or posttraumatic) adj2 (disorder* or neuros*)).tw.
71. ((psycho* or sociopath*) adj (disorder* or personalit*)).tw.
72. psychos*.tw.
73. PTSD*.tw.
74. (rett* adj (syndrome* or disorder*)).tw.
75. (self adj (destruct* or harm* or injur* or mutilat*)).tw.
76. (schizo affect* or schizoaffect*).tw.
77. schizophreni*.tw.
78. shell shock*.tw.
79. (sleep adj2 (disorder* or dysfunction*)).tw.
80. stress disorder*.tw.
81. tourette*.tw.
82. tic disorder*.tw.
83. unstable mood*.tw.
84. violen*.tw.
85. or/1-84
86. Neuroleptic Drugs/
87. Phenothiazine Derivatives/
88. (abilify or adasuve or aldazine or anatensol or anti naus).mp.
89. (anti psychotic* or antipsychotic*).mp.
90. (aripiprazole or arizole or asenapine or atrolak or biquelle).mp.
91. (brexpiprazole or buccastem or calmazine or cariprazine or chloractil).mp.
92. (chlorpromanyl or chlorpromazine or clopine or clozapine or clozaril).mp.
93. (compazine or compro or decazate or delucon or denzapine).mp.
94. (dozic or droleptan or droperidol or ebesque or fanapt).mp.
95. (fazaclo or fazalco or fentazin or fluphenazine or fortunan).mp.
96. (geodon or haldol or halo peridol or haloperidol or halperon).mp.
97. (iloperidone or inapsine or invega or lanzek or largactil).mp.
98. (latuda or loxapac or loxapine or loxitane or lurasidone).mp.

99. (major adj (tranquili?er* or tranquilli?er*)).mp.
100. (mellaril* or melleril or mintreleq or moban or modecate).mp.
101. (moditen or molindone or nausetil or navane).mp.
102. neuroleptic*.mp.
103. (novo adj (flurazine or peridol or ridazine or trifluzine)).mp.
104. (nu prochlor or olanzaccord or olanzapine or orap or ormazine).mp.
105. (ozidal or ozin or paliperidone or permitil or perphenazine).mp.
106. (pimozide or procalm or prochlorazine or prochlorperazine or procomp).mp.
107. (prolixin or promapar or prorazin or protran or proziere).mp.
108. (prozine or quetiapine or quetiaccord or quetin or resdone).mp.
109. (rexulti or rideril or rispa or risperdal or risperidone).mp.
110. (rispernia or rixadone or saphris or seotiapim or sequase).mp.
111. (serenace or seronia or seroquel or solazine or sonazine).mp.
112. (sondate or stelazine or stemetil or stemzine or sycrest).mp.
113. (syquet or terfluzine or thioridazine or thiothixene or thorazine).mp.
114. (tiotixene or trifluoperazine or trilafon or versacloz or vertigon).mp.
115. (vraylar or xeplion or xomolix or xylac or zaluron).mp.
116. (zaponex or zeldox or ziprasidone or zylap or zypadhera).mp.
117. (zypine or zyprexa).mp.
118. or/86-117
119. and/85,118
120. Adolescent Psychiatry/
121. Child Psychiatry/
122. exp Elementary School Students/
123. High School Students/
124. Junior High School Students/
125. Kindergarten Students/
126. Pediatrics/
127. adolescen*.mp.
128. (boy* or girl* or teen*).mp.
129. (child* or grade school* or kid or kids or kindergar?en* or minors* or preschool* or pre school* or school age* or schoolchild* or toddler*).mp.
130. ((colleg* or high school* or highschool* or middle school* or universit*) adj2 (age* or student*)).mp.
131. (paediatric* or peadiatric* or pediatric*).mp.
132. (prepubescen* or pubescen* or pubert*).mp.
133. (young* adj (adult* or men or mens or people* or person* or women*)).mp.
134. (youth or youths).mp.
135. or/120-134
136. and/119,135
137. Drug Therapy/
138. exp Experimental Design/
139. Observation Methods/
140. Treatment Effectiveness Evaluation/
141. (case control or cohort* or follow up or followup or longitudinal or prospective* or retrospective).tw.

142. ((compari* or epidemiologic* or experimental or observational) adj2 (analy* or study or studies)).tw.
143. groups.ab.
144. placebo.ab.
145. random*.ab.
146. trial.ab.
147. or/137-146
148. exp animals/ not humans.sh.
149. 147 not 148
150. and/136,149
151. limit 150 to English

Table B6. Dissertations and Theses International
Database: ProQuest Dissertations & Theses Global
Search Title: Antipsychotics_Child_Update
Date Searched: 22 Oct 2015
Results: 51

((su.Exact("addictions" OR "addictive behaviors" OR "alcohol use" OR "alcoholism" OR "anorexia" OR "attention deficit disorder" OR "autism" OR "behavioral psychology" OR "bipolar disorder" OR "bulimia" OR "drug abuse" OR "drug addiction" OR "drug use" OR "eating disorders" OR "emotional disorders" OR "fear & phobias" OR "hyperactivity" OR "insomnia" OR "mental depression" OR "mental disorders" OR "panic attacks" OR "post traumatic stress disorder" OR "schizophrenia" OR "sleep disorders" OR "tourette syndrome" OR "violence") OR AB,TI(((addicti* OR compulsi* OR explosive OR impuls*) NEAR/2 (behavio* OR disorder*)) OR ADHD* OR aggressi* OR agitat* OR ((alcohol* OR drug* OR substance*) NEAR/2 (abus* OR addict* OR depend* OR disorder* OR withdrawal*)) OR (((compulsiv* OR obsessive) NEAR/1 (behavio* OR disorder* OR personalit*)) OR OCD) OR anorexi* OR anxiety OR asperger* OR "attention deficit" OR autis*) OR AB,TI((behavio* NEAR/2 (disorder* OR disturb* OR disrupt* OR illness* OR problem*)) OR "bi polar" OR (binge NEAR/1 (drink* OR eat*)) OR bipolar OR bulimi* OR ((combat OR war) NEAR/1 disorder*) OR "conduct disorder*" OR cyclothymi* OR depress*) OR AB,TI("eating disorder*" OR ((emotion* OR mood) NEAR/2 disorder) OR hyperactiv* OR hyperphagia* OR insomnia* OR irritab* OR mania* OR "off label*" OR offlabel* OR (panic* NEAR/1 (attack* OR disorder*)) OR paranoi* OR "pervasive development* disorder*" OR phobia* OR phobic OR (("post traumatic" OR posttraumatic) NEAR/2 (disorder* OR neuros*)) OR psychos* OR PTSD*) OR AB,TI("reactive disorder*" OR schizophreni* OR (self NEAR/1 (destruct* OR harm* OR injur* OR mutilat*)) OR "sleep disorder*" OR "stress disorder*" OR tourette* OR "tic disorder*" OR "unlabeled indication*" OR "unlabeled use*" OR "unstable mood*" OR violen*)) AND AB,TI("anti psychotic*" OR antipsychotic* OR aripiprazole OR asenapine OR chlorpromazine OR clozapine OR droperidol OR fluphenazine OR haloperidol OR iloperidone OR loxapine OR lurasidone OR (major NEAR/1 (tranquili?er* OR tranquilli?er*)) OR molindone OR neuroleptic* OR olanzapine OR paliperidone OR perphenazine OR pimozide OR prochlorperazine OR quetiapine OR risperidone OR thiothixene OR thioridazine OR trifluoperazine OR ziprasidone) AND ALL(adolescen* OR boy* OR child* OR girl* OR kid OR kids OR minors OR paediatric* OR pediatric* OR peadiatric* OR prepubescen* OR pubert* OR pubescen* OR "school age*" OR schoolchild* OR teen* OR (young NEAR/1 (adult* OR men

OR mens OR people* OR person* OR women*)) OR youth OR youths)) NOT ALL("animal model*" OR cadaver OR nonhuman OR primate* OR rat OR rats OR zebrafish)

Additional limits - Date: From January 01 1987 to December 31 2015; Language: English

Table B7. TOXLINE

Database: TOXLINE (Toxicology Literature Online) - http://toxnet.nlm.nih.gov/cgi-bin/sis/search2
Search Title: N/A
Date Searched: 22 Oct 2015
Results: 183

Advanced Search
Search Term: exact words
Records with: all the words
Search Fields: all fields
Do not – add chemical synonyms and CAS numbers to search
Do not – include PubMed records
No maximum number of results specified
Year of publication: 1987 through 2015
Language: English

1. (adjustment disorders [mh] OR anorexia [mh] OR anxiety [mh] OR anxiety disorders [mh] OR "Attention Deficit and Disruptive Behavior Disorders" [mh] OR behavioral symptoms [mh] OR child behavior disorders [mh] OR child development disorders, pervasive [mh] OR eating disorders [mh] OR hyperphagia [mh] OR impulse control disorders [mh] OR impulsive behavior [mh] OR irritable mood [mh] OR mental disorders [mh] OR mood disorders [mh] OR "off-label use" [mh] OR psychomotor agitation [mh] OR rett syndrome [mh] OR "schizophrenia and disorders with psychotic features" [mh] OR schizophrenia, childhood [mh] OR sleep disorders [mh] OR substance-related disorders [mh] OR tic disorders [mh] OR violence [mh])

2. (ADHD* [ab] OR "attention deficit" [ab] OR "adjustment disorder*" [ab] OR "affective disorder*" [ab] OR aggressi* [ab] OR agitat* [ab] OR "alcohol abuse" [ab] OR "alcohol addiction*" [ab] OR anorexi* [ab] OR anxiety [ab] OR autis* [ab] OR asperger* [ab] OR "bi polar" [ab] OR bipolar [ab] OR bulimi* [ab] OR "compulsive behavior*" [ab] OR "compulsive behaviour*" [ab] OR "compulsive disorder*" [ab] OR depress* [ab] OR "disintegrative disorder" OR "drug abuse" [ab] OR "drug addiction*" [ab] OR "eating disorder*" [ab])

3. (hyperactiv* [ab] OR insomnia [ab] OR irritab* [ab] OR "minimal brain dysfunction" [ab] OR "off label" [ab] OR offlabel [ab] OR "panic attack*" [ab] OR "pervasive development disorder" [ab] OR "post traumatic" [ab] OR posttraumatic [ab] OR psychos* [ab] OR PTSD* [ab] OR "schizo affect*" [ab] OR schizoaffect* [ab] OR schizophreni* [ab] OR"self harm" [ab] OR "self injury" [ab] OR "self mutilation" [ab] OR "sleep disorder*" [ab] OR "stress disorder*" [ab] OR "substance abuse" [ab] OR "substance addiction" [ab] OR tourette* [ab] OR "tic disorder*" [ab] OR "unlabeled indication*" [ab] OR "unlabeled use*" [ab] OR violen* [ab])

4. #1 OR #2 OR #3

5. (antipsychotic agents [mh] OR butyrophenones [mh] OR phenothiazines [mh] OR thioxanthenes [mh] OR antipsychotic* OR aripiprazole OR asenapine OR chlorpromazine OR clozapine OR droperidol OR fluphenazine OR haloperidol OR iloperidone OR loxapine OR lurasidone OR molindone OR neuroleptic* OR olanzapine OR paliperidone OR perphenazine OR pimozide OR prochlorperazine OR quetiapine OR risperidone OR thiothixene OR thioridazine OR trifluoperazine OR ziprasidone)

6. #4 AND #5

7. (adolescent [mh] OR child [mh] OR pediatrics [mh] OR young adult [mh] OR adolescen* [ab] OR child* [ab] OR paediatric* [ab] OR pediatric* [ab] OR teen* [ab] OR "young adult*" [ab])

8. #6 AND #7

9. (animals [mh] OR bovine [ti] OR mice [ti] OR mouse [ti] OR nonhuman [ti] OR pig [ti] OR pigs [ti] OR porcine [ti] OR rabbit* [ti] OR rat [ti] OR rats [ti] OR zebrafish [ti])

10. #8 NOT #9

Table B8. ClinicalTrials.gov

Registry: ClinicalTrials.gov - https://clinicaltrials.gov/
Search Title: N/A
Date Searched: 26 Oct 2015
Results: 1498

Advanced Search

(1.) First Received: From 01/01/1987 to 12/31/2015
Targeted Search –

Conditions by category > Behaviors and Mental Disorders
"Adjustment Disorders" OR "Affective Disorders, Psychotic" OR "Affective Symptoms" OR Aggression OR Agoraphobia OR "Alcohol Drinking" OR "Alcohol-Related Disorders" OR Alcoholism OR "Anorexia Nervosa" OR "Anxiety Disorders" OR "Asperger Syndrome"

Interventions >
antipsychotics OR "anti psychotics" OR aripiprazole OR asenapine OR brexpiprazole OR cariprazine OR chlorpromazine OR clozapine OR droperidol OR fluphenazine OR haloperidol OR iloperidone OR loxapine OR lurasidone OR molindone OR olanzapine

Age Group: Child (birth -17)
Results: 104

(2.) First Received: From 01/01/1987 to 12/31/2015
Targeted Search –

Conditions by category > Behaviors and Mental Disorders
"Adjustment Disorders" OR "Affective Disorders, Psychotic" OR "Affective Symptoms" OR Aggression OR Agoraphobia OR "Alcohol Drinking" OR "Alcohol-Related Disorders" OR Alcoholism OR "Anorexia Nervosa" OR "Anxiety Disorders" OR "Asperger Syndrome"

Interventions>
paliperidone OR perphenazine OR pimozide OR prochlorperazine OR quetiapine OR risperidone OR thiothixene OR thioridazine OR trifluoperazine OR ziprasidone

Age Group: Child (birth -17)
Results: 51

(3.) First Received: From 01/01/1987 to 12/31/2015
Targeted Search –

Conditions by category > Behaviors and Mental Disorders
"Attention Deficit Disorder with Hyperactivity" OR "Attention Deficit and Disruptive Behavior Disorders" OR "Autistic Disorder" OR "Behavior, Addictive" OR " Behavioral Symptoms" OR "Binge Drinking" OR "Bipolar Disorder" OR " Bulimia Nervosa"

Interventions >
antipsychotics OR "anti psychotics" OR aripiprazole OR asenapine OR brexpiprazole OR cariprazine OR chlorpromazine OR clozapine OR droperidol OR fluphenazine OR haloperidol OR iloperidone OR loxapine OR lurasidone OR molindone OR olanzapine

Age Group: Child (birth -17)
Results: 144

(4.) First Received: From 01/01/1987 to 12/31/2015
Targeted Search –

Conditions by category > Behaviors and Mental Disorders
"Attention Deficit Disorder with Hyperactivity" OR "Attention Deficit and Disruptive Behavior Disorders" OR "Autistic Disorder" OR "Behavior, Addictive" OR " Behavioral Symptoms" OR "Binge Drinking" OR "Bipolar Disorder" OR " Bulimia Nervosa"

Interventions >
paliperidone OR perphenazine OR pimozide OR prochlorperazine OR quetiapine OR risperidone OR thiothixene OR thioridazine OR trifluoperazine OR ziprasidone

Age Group: Child (birth -17)
Results: 68

(5.) First Received: From 01/01/1987 to 12/31/2015
Targeted Search –

Conditions by category > Behaviors and Mental Disorders
"Child Behavior Disorders" OR " Child Development Disorders, Pervasive" OR " Cocaine-Related Disorders" OR " Combat Disorders" OR "Compulsive Behavior" OR "Conduct Disorder" OR "Cyclothymic Disorder" OR Depression OR "Depressive Disorder"

Interventions >
antipsychotics OR "anti psychotics" OR aripiprazole OR asenapine OR brexpiprazole OR cariprazine OR chlorpromazine OR clozapine OR droperidol OR fluphenazine OR haloperidol OR iloperidone OR loxapine OR lurasidone OR molindone OR olanzapine

Age Group: Child (birth -17)
Results: 66

(6.) First Received: From 01/01/1987 to 12/31/2015
Targeted Search –

Conditions by category > Behaviors and Mental Disorders
"Child Behavior Disorders" OR " Child Development Disorders, Pervasive" OR " Cocaine-Related Disorders" OR " Combat Disorders" OR "Compulsive Behavior" OR "Conduct Disorder" OR "Cyclothymic Disorder" OR Depression OR "Depressive Disorder"

Interventions >
paliperidone OR perphenazine OR pimozide OR prochlorperazine OR quetiapine OR risperidone OR thiothixene OR thioridazine OR trifluoperazine OR ziprasidone

Age Group: Child (birth -17)
Results: 31

(7.) First Received: From 01/01/1987 to 12/31/2015
Targeted Search –

Conditions by category > Behaviors and Mental Disorders
"Depressive Disorder, Major" OR " Depressive Disorder, Treatment-Resistant" OR "Dissociative Disorders" OR "Drinking Behavior" OR "Drug-Seeking Behavior" OR Dyssomnias OR "Dysthymic Disorder" OR "Eating Disorders"

Interventions >
antipsychotics OR "anti psychotics" OR aripiprazole OR asenapine OR brexpiprazole OR cariprazine OR chlorpromazine OR clozapine OR droperidol OR fluphenazine OR haloperidol OR iloperidone OR loxapine OR lurasidone OR molindone OR olanzapine

Age Group: Child (birth -17)
Results: 17

(8.) First Received: From 01/01/1987 to 12/31/2015

Targeted Search –

Conditions by category > Behaviors and Mental Disorders
"Depressive Disorder, Major" OR " Depressive Disorder, Treatment-Resistant" OR "Dissociative Disorders" OR "Drinking Behavior" OR "Drug-Seeking Behavior" OR Dyssomnias OR "Dysthymic Disorder" OR "Eating Disorders"

Interventions >
paliperidone OR perphenazine OR pimozide OR prochlorperazine OR quetiapine OR risperidone OR thiothixene OR thioridazine OR trifluoperazine OR ziprasidone

Age Group: Child (birth -17)
Results: 5

(9.) First Received: From 01/01/1987 to 12/31/2015
Targeted Search –

Conditions by category > Behaviors and Mental Disorders
"Feeding and Eating Disorders of Childhood" OR "Heroin Dependence" OR "Impulse Control Disorders" OR "Impulsive Behavior" OR "Marijuana Abuse" OR "Mental Disorders" OR "Mental Disorders Diagnosed in Childhood" OR "Mood Disorders"

Interventions >
antipsychotics OR "anti psychotics" OR aripiprazole OR asenapine OR brexpiprazole OR cariprazine OR chlorpromazine OR clozapine OR droperidol OR fluphenazine OR haloperidol OR iloperidone OR loxapine OR lurasidone OR molindone OR olanzapine

Age Group: Child (birth -17)
Results: 272

(10.) First Received: From 01/01/1987 to 12/31/2015
Targeted Search –

Conditions by category > Behaviors and Mental Disorders
"Feeding and Eating Disorders of Childhood" OR "Heroin Dependence" OR "Impulse Control Disorders" OR "Impulsive Behavior" OR "Marijuana Abuse" OR "Mental Disorders" OR "Mental Disorders Diagnosed in Childhood" OR "Mood Disorders"

Interventions >
paliperidone OR perphenazine OR pimozide OR prochlorperazine OR quetiapine OR risperidone OR thiothixene OR thioridazine OR trifluoperazine OR ziprasidone

Age Group: Child (birth -17)
Results: 130

(11.) First Received: From 01/01/1987 to 12/31/2015

Targeted Search –

Conditions by category > Behaviors and Mental Disorders
"Obsessive-Compulsive Disorder" OR "Opioid-Related Disorders" OR "Panic Disorder" OR Parasomnias OR "Phobic Disorders" OR "Psychomotor Agitation" OR "Psychotic Disorders" OR Schizophrenia OR "Schizophrenia and Disorders with Psychotic Features"

Interventions >
antipsychotics OR "anti psychotics" OR aripiprazole OR asenapine OR brexpiprazole OR cariprazine OR chlorpromazine OR clozapine OR droperidol OR fluphenazine OR haloperidol OR iloperidone OR loxapine OR lurasidone OR molindone OR olanzapine

Age Group: Child (birth -17)
Results: 279

(12.) First Received: From 01/01/1987 to 12/31/2015
Targeted Search –

Conditions by category > Behaviors and Mental Disorders
"Obsessive-Compulsive Disorder" OR "Opioid-Related Disorders" OR "Panic Disorder" OR Parasomnias OR "Phobic Disorders" OR "Psychomotor Agitation" OR "Psychotic Disorders" OR Schizophrenia OR "Schizophrenia and Disorders with Psychotic Features"

Interventions >
paliperidone OR perphenazine OR pimozide OR prochlorperazine OR quetiapine OR risperidone OR thiothixene OR thioridazine OR trifluoperazine OR ziprasidone

Age Group: Child (birth -17)
Results: 133

(13.) First Received: From 01/01/1987 to 12/31/2015
Targeted Search –

Conditions by category > Behaviors and Mental Disorders
"Schizophrenia and Disorders with Psychotic Features" OR "Schizophrenia, Childhood" OR "Schizophrenia, Disorganized" OR "Schizophrenia, Paranoid" OR "Schizotypal Personality Disorder" OR "Self Mutilation" OR "Self-Injurious Behavior"

Interventions >
antipsychotics OR "anti psychotics" OR aripiprazole OR asenapine OR brexpiprazole OR cariprazine OR chlorpromazine OR clozapine OR droperidol OR fluphenazine OR haloperidol OR iloperidone OR loxapine OR lurasidone OR molindone OR olanzapine

Age Group: Child (birth -17)
Results: 118

(14.) First Received: From 01/01/1987 to 12/31/2015
Targeted Search –

Conditions by category > Behaviors and Mental Disorders
"Schizophrenia and Disorders with Psychotic Features" OR "Schizophrenia, Childhood" OR "Schizophrenia, Disorganized" OR "Schizophrenia, Paranoid" OR "Schizotypal Personality Disorder" OR "Self Mutilation" OR "Self-Injurious Behavior"

Interventions >
paliperidone OR perphenazine OR pimozide OR prochlorperazine OR quetiapine OR risperidone OR thiothixene OR thioridazine OR trifluoperazine OR ziprasidone

Age Group: Child (birth -17)
Results: 53

(15.) First Received: From 01/01/1987 to 12/31/2015
Targeted Search –

Conditions by category > Behaviors and Mental Disorders
"Sleep Disorders" OR "Stress Disorders, Post-Traumatic" OR "Stress Disorders, Traumatic" OR "Stress Disorders, Traumatic, Acute" OR "Substance-Related Disorders" OR "Suicidal Ideation" OR "Tic Disorders" OR "Tourette Syndrome"

Interventions >
antipsychotics OR "anti psychotics" OR aripiprazole OR asenapine OR brexpiprazole OR cariprazine OR chlorpromazine OR clozapine OR droperidol OR fluphenazine OR haloperidol OR iloperidone OR loxapine OR lurasidone OR molindone OR olanzapine

Age Group: Child (birth -17)
Results: 22

(16.) First Received: From 01/01/1987 to 12/31/2015
Targeted Search –

Conditions by category > Behaviors and Mental Disorders
"Sleep Disorders" OR "Stress Disorders, Post-Traumatic" OR "Stress Disorders, Traumatic" OR "Stress Disorders, Traumatic, Acute" OR "Substance-Related Disorders" OR "Suicidal Ideation" OR "Tic Disorders" OR "Tourette Syndrome"

Interventions >
paliperidone OR perphenazine OR pimozide OR prochlorperazine OR quetiapine OR risperidone OR thiothixene OR thioridazine OR trifluoperazine OR ziprasidone

Age Group: Child (birth -17)
Results: 5

Total records downloaded: 1498
Total unique records: 295

Table B9. WHO ICTRP

Registry: WHO International Clinical Trials Registry Platform
Search Title: N/A
Date Searched: 27 Oct 2015
Results: 317

Advanced Search
(1.)
Search for clinical trials in children (0-18)
Recruitment status is: ALL
Intervention >
antipsychotics OR aripiprazole OR asenapine OR brexpiprazole OR cariprazine OR chlorpromazine OR clozapine OR droperidol OR fluphenazine OR haloperidol OR iloperidone OR loxapine OR lurasidone OR molindone OR olanzapine
Results: 153

(2.)
Search for clinical trials in children (0-18)
Recruitment status is: ALL
Intervention >
paliperidone OR perphenazine OR pimozide OR prochlorperazine OR quetiapine OR risperidone OR thiothixene OR thioridazine OR trifluoperazine OR ziprasidone
Results: 164

Appendix C. Quality Assessment Ratings

Table C1. Risk of Bias Assessments for Trials
Table C2. Quality Assessment Ratings for Observational Studies Using Newcastle-Ottawa Scale

References for Appendix C found at the end of Appendix D.

Table C1. Risk of Bias Assessments for Trials

Author, Year	Sequence generation	Allocation concealment	Blinding-PP (Subjective)	Blinding-PP (Objective)	Blinding-OA (Subjective)	Blinding-OA (Objective)	Incomplete outcome (Subjective)	Incomplete outcome (Objective)	Other sources of bias	Overall (Subjective)	Overall (Objective)
Aman et al., 1991 [1]	Yes	Unclear	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear
Aman et al., 2002 [2]	Yes	Unclear	Yes	Yes	N/A	Unclear	No	No	Yes	High	High
Aman et al., 2009 [3]	Yes	Unclear	Yes	Yes	N/A	N/A	Yes	Yes	Yes	Unclear	Unclear
Aman et al., 2014 [4]	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear
Anderson et al., 1989 [5]	Unclear	Unclear	Yes	Yes	Yes	Yes	No	Yes	Unclear	High	Unclear
Arango et al., 2009 [6]	Unclear	Unclear	No	No	No	No	No	No	Yes	High	High
Armenteros et al., 2007 [7]	Yes	Unclear	Unclear	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear	Unclear
Berger et al., 2008 [8]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low	Low
Biederman et al., 2005 [9]	Unclear	Unclear	No	No	Unclear	Unclear	No	No	Yes	High	High
Bruggeman et al., 2001 [10]	Yes	Unclear	NA	Yes	NA	Unclear	NA	Yes	Yes	NA	Unclear
Buchsbaum et al., 2007 [11]	Unclear	Unclear	Unclear	NA	Unclear	NA	Unclear	NA	Yes	Unclear	NA
Buitelaar et al., 2001 [12]	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear
Connor et al., 2008 [13]	Unclear	Yes	Yes	Yes	NA	Yes	No	No	Yes	High	High

Author, Year	Sequence generation	Allocation concealment	Blinding-PP (Subjective)	Blinding-PP (Objective)	Blinding-OA (Subjective)	Blinding-OA (Objective)	Incomplete outcome (Subjective)	Incomplete outcome (Objective)	Other sources of bias	Overall (Subjective)	Overall (Objective)
Crocq et al., 2007 [14]	No	No	NA	Yes	NA	Yes	NA	Unclear	Unclear	NA	High
de Haan et al., 2003 [15]	Yes	Unclear	Unclear	Unclear	Unclear	Unclear	No	No	Yes	High	High
DelBello et al., 2002 [16]	Yes	Yes	Unclear	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear	Unclear
DelBello et al., 2008 [17]	Unclear	Unclear	No	Unclear	Unclear	Unclear	No	No	Yes	High	High
DelBello et al., 2009 [18]	Yes	Yes	Unclear	Unclear	Unclear	Unclear	No	No	Yes	High	High
Findling et al., 2000 [19]	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	High	High
Findling et al., 2008a [20]	Yes	Unclear	Unclear	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear	Unclear
Findling et al., 2009 [21]	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear
Findling et al., 2012a [22]	Yes	Unclear	Yes	Yes	Yes	Yes	No	No	No	High	High
Findling et al., 2012b [23]	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	No	No	No	High	High
Findling et al., 2013a [24]	Unclear	Unclear	Unclear	Yes	Unclear	Yes	No	No	Unclear	High	High
Findling et al., 2013b [25]	Unclear	Unclear	Unclear	Yes	Unclear	Yes	No	No	Unclear	High	High
Findling et al., 2014a [26]	Yes	Unclear	Unclear	Unclear	Unclear	Unclear	No	No	Yes	High	High
Findling et al., 2014b [27]	Unclear	Yes	Unclear	Unclear	Unclear	Unclear	No	No	Yes	High	High

Author, Year	Sequence generation	Allocation concealment	Blinding-PP (Subjective)	Blinding-PP (Objective)	Blinding-OA (Subjective)	Blinding-OA (Objective)	Incomplete outcome (Subjective)	Incomplete outcome (Objective)	Other sources of bias	Overall (Subjective)	Overall (Objective)
Findling et al., 2015a [28]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low	Low
Findling et al., 2015b [29]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low	Low
Ghanizadeh et al., 2014a [30]	Unclear	Unclear	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear
Ghanizadeh et al., 2014b [31]	Yes	Unclear	Unclear	Yes	Yes	Yes	No	No	Unclear	High	High
Gilbert et al., 2004 [32]	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	High	High
Gulisano et al., 2011 [33]	Unclear	Unclear	NA	Yes	NA	Yes	NA	Yes	Yes	NA	Unclear
Haas et al., 2009a [34]	Yes	Unclear	Unclear	Yes	Unclear	Yes	No	No	Yes	High	High
Haas et al., 2009b [35]	Yes	Unclear	Unclear	N/A	Unclear	Yes	No	No	Yes	High	High
Haas et al., 2009c [36]	Unclear	Unclear	Unclear	Yes	Unclear	Yes	No	No	Yes	High	High
Hagman et al., 2011 [37]	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear
Hellings et al., 2006 [38]	Unclear	Yes	Unclear	Yes	Unclear	Yes	No	No	No	High	High
Hollander et al., 2006 [39]	Unclear	Unclear	Unclear	Yes	Unclear	Yes	No	No	Yes	High	High
Jensen et al., 2008 [40]	Yes	Unclear	No	Yes	No	Yes	No	No	Yes	High	High
Johnson & Johnson, 2011 [41]	Unclear	Unclear	No	No	No	No	Yes	Yes	Yes	High	High

Author, Year	Sequence generation	Allocation concealment	Blinding-PP (Subjective)	Blinding-PP (Objective)	Blinding-OA (Subjective)	Blinding-OA (Objective)	Incomplete outcome (Subjective)	Incomplete outcome (Objective)	Other sources of bias	Overall (Subjective)	Overall (Objective)
Kafantaris et al., 2011 [42]	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear
Kent et al., 2013 [43]	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear
Kowatch et al., 2015 [44]	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear	Unclear
Kryzhanovskaya et al., 2009 [45]	Unclear	Unclear	Unclear	Yes	Unclear	Yes	No	No	Yes	High	High
Kumra et al., 1996 [46]	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	High	High
Kumra et al., 2008 [47]	Yes	Yes	Unclear	Yes	Unclear	Yes	No	No	Yes	High	High
Luby et al., 2006 [48]	Yes	Yes	Unclear	Yes	Unclear	Yes	Yes	Yes	Yes	Unclear	Low
Malone et al., 2001 [49]	Yes	Unclear	No	Yes	No	Yes	Yes	Yes	Yes	High	Unclear
Marcus et al., 2009 [50]	Yes	Yes	Unclear	Yes	Unclear	Yes	No	No	Yes	High	High
Masi et al., 2013 [51]	Unclear	No	No	Yes	No	Yes	Yes	Yes	Yes	High	Unclear
Masi et al., 2015 [52]	Unclear	Unclear	No	No	No	No	Yes	Yes	Yes	High	High
McCracken et al., 2002 [53]	Yes	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear
McGorry et al., 2013 [54]	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	High	High
Miral et al., 2008 [55]	Unclear	Unclear	Unclear	Yes	Unclear	Yes	Yes	Yes	Yes	Unclear	Unclear

Author, Year	Sequence generation	Allocation concealment	Blinding-PP (Subjective)	Blinding-PP (Objective)	Blinding-OA (Subjective)	Blinding-OA (Objective)	Incomplete outcome (Subjective)	Incomplete outcome (Objective)	Other sources of bias	Overall (Subjective)	Overall (Objective)
Mozes et al., 2006 [56]	Unclear	Unclear	No	Yes	No	Yes	No	No	Yes	High	High
Nagaraj et al., 2006 [57]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low	Low
NCT00194012, 2013 [58]	Unclear	Unclear	Yes	Yes	Yes	Yes	No	No	Yes	High	High
NCT01149655, 2014 [59]	Unclear	Unclear	Yes	Yes	Yes	Yes	No	No	No	High	High
Omranifard et al., 2013 [60]	Unclear	Unclear	No	NA	No	NA	Yes	NA	Yes	High	NA
Owen et al., 2009 [61]	Yes	Yes	Unclear	Yes	Unclear	Yes	Yes	Yes	Yes	Unclear	Low
Pathak et al., 2013 [62]	Yes	Yes	Yes	Yes	Unclear	Unclear	No	No	Yes	High	High
Perry et al., 1989 [63]	Unclear	Unclear	Yes	Yes	Yes	Yes	No	No	Yes	High	High
Remington et al., 2001 [64]	Yes	Unclear	Yes	Yes	Unclear	Unclear	Yes	Yes	No	High	High
Reyes et al., 2006 [65]	Unclear	Unclear	Yes	Yes	Yes	Yes	No	No	Yes	High	High
Rizzo et al., 2012 [66]	No	No	No	Yes	No	Yes	Yes	Yes	Yes	High	High
RUPP et al., 2005 [67]	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear	Unclear
Sallee et al., 1994 [68]	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Yes	Unclear	Unclear
Sallee et al., 1997 [69]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	High	High

Author, Year	Sequence generation	Allocation concealment	Blinding-PP (Subjective)	Blinding-PP (Objective)	Blinding-OA (Subjective)	Blinding-OA (Objective)	Incomplete outcome (Subjective)	Incomplete outcome (Objective)	Other sources of bias	Overall (Subjective)	Overall (Objective)
Sallee et al., 2000 [70]	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear	Unclear
Savitz et al., 2015 [71]	Yes	Unclear	Unclear	Yes	Unclear	Yes	Yes	Yes	Yes	Unclear	Unclear
Scahill et al., 2003 [72]	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear
Schneider et al., 2012 [73]	Unclear	Unclear	Unclear	Yes	Unclear	Yes	No	No	No	High	High
Sehgal et al., 1999 [74]	Unclear	Yes	Yes	NA	Yes	NA	Yes	NA	Yes	Unclear	NA
Shaw et al., 2006 [75]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Unclear
Shea et al., 2004 [76]	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear	Unclear
Sikich et al., 2004 [77]	Yes	Unclear	Yes	NA	Yes	NA	No	No	Yes	High	High
Sikich et al., 2008 [78]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low	Low
Singh et al., 2011 [79]	Unclear	Unclear	No	Yes	No	Yes	Yes	Yes	Yes	High	Unclear
Snyder et al., 2002 [80]	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	High	High
Spencer et al., 1994 [81]	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Yes	Yes	Unclear	Unclear	Unclear
Stocks et al., 2012 [82]	Unclear	Unclear	Unclear	Yes	Unclear	Yes	No	No	Yes	High	High
Swadi et al., 2010 [83]	Yes	Unclear	No	Yes	No	Yes	No	No	Yes	High	High

Author, Year	Sequence generation	Allocation concealment	Blinding-PP (Subjective)	Blinding-PP (Objective)	Blinding-OA (Subjective)	Blinding-OA (Objective)	Incomplete outcome (Subjective)	Incomplete outcome (Objective)	Other sources of bias	Overall (Subjective)	Overall (Objective)
Tohen et al., 2007 [84]	Unclear	Unclear	Unclear	Yes	Unclear	Yes	Yes	Yes	Yes	Unclear	Unclear
Tramontina et al., 2009 [85]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low	Low
Troost et al., 2005 [86]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low	Low
Van Bellinghen et al., 2001 [87]	Unclear	Unclear	Unclear	Yes	Unclear	Yes	Yes	Yes	Yes	Unclear	Unclear
Van Bruggen et al., 2003 [88]	Unclear	Unclear	Unclear	Yes	Unclear	Yes	Yes	Yes	No	High	High
Woods et al., 2003 [89]	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	High	High
Yen et al., 2004 [90]	Unclear	Unclear	Unclear	Yes	Unclear	Yes	No	No	Yes	High	High
Yoo et al., 2011 [91]	No	No	No	Yes	No	Yes	No	No	Yes	High	High
Yoo et al., 2013 [92]	Yes	Unclear	Yes	Yes	Yes	Yes	No	No	Yes	High	High

Blinding of OA = blinding of outcome assessors; Blinding of PP = blinding of participants and personnel; NA = not applicable

Table C2. Quality Assessment Ratings for Observational Studies Using Newcastle-Ottawa Scale

Author, Year Study design	Selection 1	Selection 2	Selection 3	Comparability	Outcome 1	Outcome 2	Outcome 3	Total Stars
Alacqua et al., 2008 [93] RCS	B	A	A	C	B	A	A	6
Aman et al., 2004 [94] PCS	A	A	B	A and B	A	A	C	7
Arango et al., 2014 [95] PCS	A	A	C	A and B	D	A	C	5
Bastiaens et al., 2009 [96] RCS	B	A	A	A and B	E	A	C	6
Bobo et al., 2013 [97] RCS	A	A	A	A and B	A	A	A	8
Calarge et al., 2014 [98] PCS	D	A	A	A	B	A	C	5
Castro-Fornieles et al., 2008 [99] PCS	A	A	B	A and B	D	A	C	6
Cianchetti et al., 2011 [100] PCS	A	A	B	C	D	A	B	5
Correll et al., 2009 [101] PCS	A	A	A	A and B	B	A	A	8
Cuerda et al., 2011 [102]	A	A	D	A	B	A	C	6

Author, Year Study design	Selection 1	Selection 2	Selection 3	Comparability	Outcome 1	Outcome 2	Outcome 3	Total Stars
PCS								
Ebert et al., 2014 [103] RCS	A	A	A	C	D	A	A	5
Findling et al., 2008b [104] PCS	B	A	A	C	C	A	B	5
Fleischhaker et al., 2006 [105] PCS	D	C	B	C	E	A	A	3
Fraguas et al., 2008 [106] PCS	A	A	A	A and B	D	A	C	6
Friedlander et al., 2001 [107] RCS	C	A	A	C	E	A	A	4
Germano et al., 2014 [108] PCS	A	A	A	C	D	A	B	5
Gothelf et al., 2002 [109] PCS	C	C	A	C	B	A	D	3
Hrdlicka et al., 2009 [110] RCS	A	A	A	C	B	A	C	5
Jerrell et al., 2008 [111] RCS	A	A	A	C	B	A	A	6
Khan et al., 2009 [112]	A	A	A	C	B	A	A	6

Author, Year **Study design**	**Selection 1**	**Selection 2**	**Selection 3**	**Comparability**	**Outcome 1**	**Outcome 2**	**Outcome 3**	**Total Stars**
RCS								
Khan et al., 2006 [113] RCS	D	C	A	C	B	A	A	4
Kumra et al., 1998 [114] PCS	B	A	B	C	E	A	A	5
Mankoski et al., 2013 [115] PCS	A	A	D	A and B	D	A	A	6
Martin et al., 2000 [116] PCS	A	A	A	C	B	A	A	6
Migliardi et al., 2009 [117] RCS	B	A	A	B	B	A	A	7
NCT00619190, 2013 [118] PCS	A	C	B	C	D	A	B	4
Norris et al., 2011 [119] RCS	A	A	A	A and B	B	A	A	7
Novaes et al., 2008 [120] RCS	A	A	A	A and B	B	A	A	8
O'Donoghue et al., 2014 [121] PCS	A	A	D	C	D	A	C	3
Oh et al., 2013 [122]	A	A	A	B	B	A	C	6

Author, Year Study design	Selection 1	Selection 2	Selection 3	Comparability	Outcome 1	Outcome 2	Outcome 3	Total Stars
PCS								
Olfson et al., 2012 [123] RCS	A	A	A	A	B	A	A	7
Pandina et al., 2007 [124] PCS	A	A	D	A and B	D	A	A	6
Pogge et al., 2005 [125] RCS	A	A	A	C	A	A	A	6
Ratzoni et al., 2002 [126] PCS	D	C	B	C	E	A	A	3
Saito et al., 2004 [127] PCS	B	A	A	B	D	A	A	6
Weisler et al., 2011 [128] RCS	A	A	A	A and B	D	A	B	6
Wink et al., 2014 [129] RCS	A	A	A	B	B	A	A	7
Wonodi et al., 2007 [130] RCS	A	A	A	A and B	A	A	A	8
Wudarsky et al., 1999 [131] PCS	A	A	A	A	A	A	A	7

PCS = prospective cohort study; RCS = retrospective cohort study

Appendix D. Study Characteristics

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Alacqua et al., 2008 [93] **Country:** Italy **Condition category:** Mixed conditions (ADHD, ASD, schizophrenia-related, tics) **Funding:** NR **Newcastle-Ottawa Scale:** 6/8 stars	**Recruitment dates:** Jan 2002 to Dec 2003 **Study design:** Retrospective cohort **Diagnostic criteria:** DSM-IV **Setting:** Outpatient/community **Inclusion criteria:** (1) ≤18 yr, (2) received an incident treatment with atypical antipsychotics or SSRIs during the study period **Exclusion criteria:** NR	**Enrolled:** 73 **Analyzed:** 73 **Completed:** 50 **GROUP 1** **N:** 2 **Age, mean±SD (range):** 15.5±0.7 **Males %:** 50 **Caucasian %:** NR **Diagnostic breakdown (n):** psychosis (1), schizophrenia (1) **Treatment naïve (n):** all **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 24 **Age, mean±SD (range):** 14.7±2.3 **Males %:** 42 **Caucasian %:** NR **Diagnostic breakdown (n):** affective disorder (2), anxiety disease (4), autism (1), CD (1), MR (3), personality disorder (2), psychosis (9), schizophrenia (2) **Treatment naïve (n):** all **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR	**Treatment duration:** 3 mo **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Clozapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 150±70.1 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 7.1±4.4 **Concurrent treatments:** NR **GROUP 3** **Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 375±318.2 **Concurrent treatments:** NR **GROUP 4** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD**	**Benefits:** NR **Harms:** Behavioral issues, dyskinesia, dystonia, dermatologic AE, liver function, hepatic volume, prolactin, prolactin-related AE, sedation, sleepness, total AE, weight change	Adverse events occurred frequently during first 3 months of treatment with atypical antipsychotics.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
			(range): 2±1.3 **Concurrent treatments:** NR		
		GROUP 3 **N:** 2 **Age, mean±SD (range):** 16.5±1.5 **Males %:** 100 **Caucasian %:** NR **Diagnostic breakdown (n):** psychosis (2) **Treatment naïve (n):** all **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 4** **N:** 45 **Age, mean±SD (range):** 13±3.9 **Males %:** 80 **Caucasian %:** NR **Diagnostic breakdown (n):** ADHD (1), anxiety disease (2), autism (14), CD (7), conversion disorder (2), MR (8), psychosis (7), schizophrenia (2), tic disorder (2) **Treatment naïve (n):** all **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR			
Aman et al., 2014 [4] **Country:** USA **Condition category:** ADHD **Funding:**	**Recruitment dates:** August 2008 – November 2012 **Study design:** RCT (parallel) **Setting:** NR	**Enrolled:** 168 **Analyzed:** 168 **Completed:** 137 **GROUP 1** **N:** 84 **Age, mean±SD (range):** 9.03±2.05 yr	**Treatment duration:** 6 wk **Run-in phase:** Yes **Run-in phase duration:** 2 wk most drugs, 4 wk antipsychotics and fluoxetine **Permitted drugs:** methylphenidate	**Benefits:** NCBRF, ABS, CGI-I, CGI-S, response **Harms:** metabolic effects, prolactin effects, sedation and sleep issues, GI,	Risperidone provided moderate but variable improvement in aggressive and other seriously disruptive child behaviors when

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Non-industry **Risk of bias:** Medium (subjective), Medium (objective)	**Diagnostic criteria:** DSM-IV **Inclusion criteria:** 6-12 yr, DSM-IV diagnosis of DBD (CD or ODD) or ADHD, serious physical aggression (Overt Aggression Scale – M ≥3), evidence of seriously disruptive behavior (parent rating NCBRF D-Total ≥ 27, CGI-S ≥ 4 by blinded clinician **Exclusion criteria:** IQ < 71, pregnancy, history of seizure disorder or neurological or medical disorder, abnormal liver function, PDD, schizophrenia or other psychotic disorders, ED, hypomanic/biphasic score ≥ 36 on GBI (mood disorder), current or previous major depressive disorder or diagnosis of bipolar disorder, current use of psychotropic medications where discontinuation would be a significant risk, active substance use disorder, current child	**Males %:** 77.4% **Caucasian %:** 57.1% **Diagnostic breakdown (n):** ADHD (84) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** CD (22), ODD (62) **GROUP 2** **N:** 84 **Age, mean±SD (range):** 8.75±1.98 yr **Males %:** 76.2% **Caucasian %:** 48.8% **Diagnostic breakdown (n):** ADHD (84) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** CD (22), ODD (62)	**Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone **Dosing variability:** Variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.7±0.75 mg/day **Concurrent treatments:** Methylphenidate, parent training (PT) **GROUP 2** **Drug name:** Placebo **Dosing variability:** Variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.9±0.72 mg/day **Concurrent treatments:** Methylphenidate, parent training (PT)	headache	added to PT and optimized stimulant treatment.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	abuse or neglect, history of suicide attempt (past year) or current suicidal ideation, family history type 2 diabetes in ≥ 2 first-degree relatives				
Aman et al., 2009 [3] **Country:** USA **Condition category:** ADHD **Funding:** NR **Risk of bias:** Medium (subjective), Medium (objective)	**Recruitment dates:** NR **Study design:** RCT (crossover) **Diagnostic criteria:** DSM-IV, IQ test (Stanford-Binet, Weschsler Intelligence, Kaufman Brief) **Setting:** Inpatient and outpatient **Inclusion criteria:** (1) 4–14 yr, (2) IQ ≤84, (3) ODD or CD, (4) dx of austistic or PDD NOS, (5) availability of a reliable informant, (6) good physical health **Exclusion criteria:** (1) presence of psychosis, (2) history of NMS, (3) history of severe drug allergy/hypersensitivity, (4) medical disease, (5) pregnancy	**Enrolled:** 16 **Analyzed:** 15 **Completed:** NR **GROUP 1** **N:** 16 (crossover) **Age, mean±SD (range):** 8.56±2.6 yr **Males %:** 87.5% **Caucasian %:** 81.2% **Diagnostic breakdown (n):** ADHD (1), ADHD + CD (2), ADHD + ODD (6), CD (1), ODD (3), ASD (3) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** Borderline intellectual disability (10), mild intellectual disability (4), moderate intellectual disability (1) **GROUP 2** **N:** 16 (crossover) **Age, mean±SD (range):** See group 1 **Males %:** See group 1 **Caucasian %:** See group 1 **Diagnostic breakdown (n):** See group 1 **Treatment naïve (n):** NR	**Treatment duration:** 4 wk **Run-in phase:** Yes **Run-in phase duration:** 1 wk **Permitted drugs: c**lonidine, lithium **Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.65±1.3 (0.4–5) **Concurrent treatments:** psychostimulants (5) **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	**Benefits:** ABC, NCBRF Cognitive (MTS, STRM, CPT, GHT) **Harms:** Dyskinesia, SBP, DBP, pulse	Risperidone may have a beneficial effect on efficiency or responding, activity level, static tremor, and aspects of behavior.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Inpatients (n): NR **First episode psychosis (n):** NR **Comorbidities (n):** See group 1			
Aman et al., 2004 [94] (see Aman 2002, Snyder 2002) **Country:** Canada, South Africa, USA **Condition category:** ADHD **Funding:** NR **Newcastle-Ottawa Scale:** 7/8 stars	**Study design:** Observational (pooled analysis)	**Enrolled:** NA **Analyzed:** 155 **Completed:** NA **GROUP 1** **N:** 43 **Age, mean±SD (range):** 8.6±2.1 yr **Males %:** 81.4% **Caucasian %:** 55.8% **Diagnostic breakdown (n):** CD, ODD, or DBD-NOS with ADHD (43) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** All have ADHD **GROUP 2** **N:** 35 **Age, mean±SD (range):** 9.0±1.7 yr **Males %:** 85.7% **Caucasian %:** 65.7% **Diagnostic breakdown (n):** CD, ODD, or DBD-NOS with ADHD (35) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** All have ADHD **GROUP 3**	**GROUP 1** **Drug name:** Risperidone (only) **Dosing variability:** Variable **Target dose (mg/day):** 0.06 mg/kg/day **Daily dose (mg/day), mean±SD (range):** 1.11 mg/day **Concurrent treatments:** See Aman 2002 and Snyder 2002 **GROUP 2** **Drug name:** Risperidone + stimulant **Dosing variability:** Variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.07 mg/day **Concurrent treatments:** See Aman 2002 and Snyder 2002 - psychostimulants **GROUP 3** **Drug name:** Placebo (only) **Dosing variability:** Variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** See Aman 2002 and Snyder 2002 **GROUP 4** **Drug name:** Placebo + stimulant **Dosing variability:** Variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** See Aman	**Benefits:** NCBRF, ABC **Harms:** metabolic effects, somnolence, headache, infections	Risperidone was a safe and effective treatment with or without stimulant added, for DBD and comorbid ADHD in children.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		N: 39 **Age, mean±SD (range):** 8.3±2.2 yr **Males %:** 74.4% **Caucasian %:** 56.4% **Diagnostic breakdown (n):** CD, ODD, or DBD-NOS with ADHD (39) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** All have ADHD **GROUP 4** **N:** 38 **Age, mean±SD (range):** 8.9±2.1 yr **Males %:** 92.1% **Caucasian %:** 73.7% **Diagnostic breakdown (n):** CD, ODD, or DBD-NOS with ADHD (38) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** All have ADHD	2002 and Snyder 2002 - psychostimulants		
Aman et al., 2002 [2] **Country:** USA **Condition category:** ADHD **Funding:** Industry **Risk of bias:** High (subjective), High	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** NR **Diagnostic criteria:** DSM-IV, NCBRF	**Enrolled:** 119 **Analyzed:** 118 **Completed:** 118 **GROUP 1** **N:** NR **Age, mean±SD (range):** 8.7±2.1 yr **Males %:** 85 **Caucasian %:** 51 **Diagnostic breakdown**	**Treatment duration:** 6 wk **Run-in phase:** Yes **Run-in phase duration:** 1 wk **Permitted drugs:** antihistamines, chloral hydrate, medication for EPS, melatonin, psychostimulants (dose stable for ≥30 day before study) **Prohibited drugs:** anticonvulsants, antidepressants, antipsychotics,	**Benefits:** ABC, BPI, CGI-I, NCBRF, VAS-MS Medication adherence, response (CGI) **Harms:** ECG changes, EPS, prolactin, prolactin-related AE, SAE,	Risperidone was well tolerated and effective in children with disturbed behaviors and subaverage intelligence.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
(objective)	**Inclusion criteria:** (1) total rating of ≥24 on the conduct problem subscale of the NCBRF, (2) dx of CD, ODD, or DBD NOS, (3) dx of subaverage IQ (≥36 and ≤84) and a VABS score ≤84, (4) patients with ADHD eligible if meeting all other criteria, (5) healthy, (6) 5–12 yr, (7) symptoms sufficiently severe for antipsychotic treatment, (8) a responsible person to accompany patient to study visits, provide reliable assessments, dispense study medication **Exclusion criteria:** (1) dx of PDD, schizophrenia, other psychotic disorders, (2) head injury as a cause of intellectual disability, (3) seizure disorder/ neuroleptics, (4) known hypersensitivity to risperidone or neuroleptics, (5) history of tardive dyskinesia or NMS, (6) serious or progressive illnesses, (7) presence of HIV, (8) use of an investigational drug within the previous 30	**(n):** CD (9), CD + ADHD (12), DBD (1) DBD + ADHD (4), ODD (12), ODD+ ADHD (17) **Treatment naïve (n):** 55 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (33), MR (borderline (32), mild (16), moderate (7)) **GROUP 2** **N:** NR **Age, mean±SD (range):** 8.1±2.3 yr **Males %:** 79 **Caucasian %:** 62 **Diagnostic breakdown (n):** CD (12), CD + ADHD (14), DBD (1) DBD + ADHD (2), ODD (13), ODD + ADHD (21) **Treatment naïve (n):** 63 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (37), MR (borderline (28), mild (22), moderate (13))	carbamazepine, cholinesterase inhibitors, lithium, medications for sleep/anxiety, valproic acid **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.2±0.6 **Concurrent treatments:** all groups: methylphenidate hydrochloride (35) **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** see group 1	sedation, total AE, WAE, weight change	

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	day, (9) previously received risperidone, (10) lab values outside of normal range unless not clinically relevant, (11) females of childbearing age, sexually active and not using birth control, (12) patients whose NCBRF conduct problem subscale score was reduced to <24 in response to a 1 wk placebo treatment before the study				
Aman et al., 1991 [1] **Country:** New Zealand **Condition category:** ADHD **Funding:** Non-industry **Risk of bias:** Medium (subjective), Medium (objective)	**Recruitment dates:** NR **Study design:** RCT (crossover) **Setting:** Outpatient **Diagnostic criteria:** DISC-P, DSM-III **Inclusion criteria:** Met criteria for ADD or CD, subnormal IQ (<76), attending special classes or special schools for mental retardation or adjustment classes for youngest children **Exclusion criteria:** NR	**Enrolled:** 30 **Analyzed:** 30 **Completed:** 30 **All participants** **N:** 30 **Age, mean±SD (range):** 10.1 (4.1-16.5) yr **Males %:** 83% **Caucasian %:** 70% **Diagnostic breakdown (n):** ADHD (24), ADD (4), ADD Residual type (1), CD (3) **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities (n):** Significantly subnormal IQ (27), PDD (1) Subjects assigned to three orders of drugs: Thioridazine,	**Treatment duration:** 9 wk (3 wk per treatment) **Run-in phase:** Yes **Run-in phase duration:** NR **Permitted drugs:** epilepsy drugs (phenytoin, carbamazepine, phenobarbital, sodium valproate) **Prohibited drugs:** All psychotropics **GROUP 1** **Drug name:** Thioridazine **Dosing variability:** Fixed **Target dose (mg/day):** 1.75 mg/kg/day **Daily dose (mg/day), mean±SD (range):** 1.75 mg/kg/day in 2 daily doses **Concurrent treatments:** Phenytoin + carbamazepine (2), Phenobarbital + **GROUP 2** **Drug name:** Placebo	**Benefits:** CTRS, RBPC, DCB, RLRS **Harms:** HR, BP, Weight, cognition	Clinical response to thioridazine was substantially less than the response to methylphenidate, with significant improvements confined to conduct and hyperactivity problems on teacher ratings.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		methylphenidate, placebo	**Dosing variability:** Fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 2 identical placebo capsules per day **Concurrent treatments:** See group 1		
Anderson et al., 1989 [5] **Country:** USA **Condition category:** ASD **Funding:** Non-Industry **Risk of bias:** High (subjective), Medium (objective)	**Recruitment dates:** NR **Study design:** RCT (crossover) **Setting:** NR **Diagnostic criteria:** DSM-III **Inclusion criteria:** (1) Dx of infantile autism using DSM III, made independently by three child psychiatrists **Exclusion criteria:** (1) Patients with history of seizure disorder, gross neurological deficit, endocrine or systematic disease, or those with an identifiable cause for autism, (2) patients rated as hypoactive and anergic on baseline	**Enrolled:** 45 **Analyzed:** 42 **Completed:** 42 **GROUP 1** **N:** 14 **Age, mean±SD (range):** see below **Males %:** see below **Caucasian %:** NR **Diagnostic breakdown (n):** autistic disorder (all) **Treatment naïve (n):** NR **Inpatients (n):** 14 **First episode psychosis (n):** NR **Comorbidities:** see below **GROUP 2** **N:** 14 **Age, mean±SD (range):** see below **Males %:** see below **Caucasian %:** NR **Diagnostic breakdown (n):** autistic disorder (all) **Treatment naïve (n):** NR **Inpatients (n):** 14 **First episode psychosis (n):** NR **Comorbidities:** see below **GROUP 3**	**Treatment duration:** 14 wk **Run–in phase:** Yes **Run–in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** RN **GROUP 1** **Drug name:** Haloperidol, Placebo, Placebo **Dosing variability:** variable **Target dose (mg/day):** 4.0 **Daily dose (mg/day), mean±SD (range):** 0.84±0.57 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo, Haloperidol, Placebo **Dosing variability:** variable **Target dose (mg/day):** 4.0 **Daily dose (mg/day), mean±SD (range):** 0.84±0.57 **Concurrent treatments:** NR **GROUP 3** **Drug name:** Placebo, Placebo, Haloperidol **Dosing variability:** variable **Target dose (mg/day):** 4.0 **Daily dose (mg/day), mean±SD (range):** 0.84±0.57 **Concurrent treatments:** NR	**Benefits:** CPRS, CGI-I, CGI-S, CGI-Efficacy, Conners PTQ, medication adherence **Harms:** sedation, acute dystonic reaction	Haloperidol did not have generalized facilitating effects on discrimination learning. However, it is important that haloperidol administration did not have an adverse effect on learning during the 4-wk period, and this itself is important information regarding a population where the majority is of subnormal intellectual functioning, having severe learning difficulties.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		N: 14 **Age, mean±SD (range):** see below **Males %:** see below **Caucasian %:** NR **Diagnostic breakdown (n):** autistic disorder (all) **Treatment naïve (n):** NR **Inpatients (n):** 14 **First episode psychosis:**NR **Comorbidities:** NR **First episode psychosis (n):** NA **Comorbidities:** see below **Overall age, mean±SD (range):** 4.49±1.16 yr **Overall males %:** 77.8 **Overall comorbidities:** mild/low level retardation (42), of these, profoundly or severely retarded (29)			
Arango et al., 2014 [95] **Country:** Spain **Condition category:** Mixed conditions **Funding:** Non-industry **Newcastle-Ottawa Scale:** 5/8 stars	**Recruitment dates:** May 2005 to Feb 2009 **Study design:** Prospective **Setting:** Inpatient/outpatient **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) 4-7 yr, (2) ≤30 days of lifetime exposure to SGAs, (3) met DSM-IV psychiatric diagnosis other than a primary	**Enrolled:** 303 **Analyzed:** 279 **Completed:** 165 (at 6mo) **GROUP 1** **N:** 157 **Age, mean±SD (range):** 14.0±3.3 yr **Males %:** 64.3 **Caucasian %:** 84.7 **Diagnostic breakdown (n):** Schizophrenia spectrum (48), mood spectrum disorders (34), behavioral disorders (42), other diagnosis (29) **Treatment naïve (n):** 80 **Inpatients (n):** see below	**Treatment duration:** 6 mo **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** Antidepressants (14), benzodiazepines (40), mood stabilizers (19), stimulants (1)	**Benefits:** NA **Harms:** Weight (BMI, BMI-z), lipid values, fasting glucose, insulin, blood pressure (systolic/ diastolic)	Close screening and monitoring of cadio-metabolic side effects (CSE) is imperative, at least during the initial months of treatment, and suggest that there are differences in CSE risk and temporal pattern with olanzapine, risperidone, and quetiapine.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	eating disorder **Exclusion criteria:** NR	**First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 44 **Age, mean±SD (range):** 15.4±1.8 yr **Males %:** 63.6 **Caucasian %:** 93.2 **Diagnostic breakdown (n):** Schizophrenia spectrum (15), mood spectrum disorders (17), behavioral disorders (5), other diagnosis (6) **Treatment naïve (n):** 14 **Inpatients (n):** see below **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 3** **N:** 47 **Age, mean±SD (range):** 15.7±1.6 yr **Males %:** 53.2 **Caucasian %:** 89.4 **Diagnostic breakdown (n):** Schizophrenia spectrum (21), mood spectrum disorders (21), behavioral disorders (0), other diagnosis (3) **Treatment naïve (n):** 24 **Inpatients (n):** see below **First episode psychosis (n):** NR **Comorbidities:** NR **Overall inpatients (n):** 200	**GROUP 2** **Drug name:** Olanzapine **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** Antidepressants (14), benzodiazepines (18), mood stabilizers (7), stimulants (0) **GROUP 3** **Drug name:** Quetiapine **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** Antidepressants (11), benzodiazepines (12), mood stabilizers (7), stimulants (0)		

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Arango et al., 2009 [6] **Country:** Spain **Condition category:** Schizophrenia and related **Funding:** Industry, Academic **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Inpatient **Diagnostic criteria:** DSM-IV, K-SADS-PL **Inclusion criteria:** (1) adolescents admitted to the hospital with psychosis (schizophrenia or any other psychotic disorder (DSM-IV)) **Exclusion criteria:** (1) psychotic symptoms appearing to result from acute intoxication or withdrawal (if psychotic symptoms did not persist after 14 day of a negative urine drug screening), (2) DSM-IV criteria for any substance abuse, MR, or PDD, (3) organic CNS disorder, (4) history of TBI with loss of consciousness, (5) IQ <70 and a clinical criterion of impaired functioning prior to the onset of the disorder, (6) pregnant or breast feeding, (7) taking olanzapine or	**Enrolled:** 50 **Analyzed:** 49 **Completed:** 32 **GROUP 1** **N:** 26 **Age, mean±SD (range):** 15.7±1.4 **Males %:** 76 **Caucasian %:** 76 **Diagnostic breakdown (n):** bipolar disorder (5), other psychoses (12: major depressive episode with psychotic features (3), psychosis NOS (4), schizoaffective disorder (3), schizophreniform disorder (2)), schizophrenia (9) **Treatment naïve (n):** 10 **Inpatients (n):** all **First episode psychosis (n):** all **Comorbidities:** psychosis (all) **GROUP 2** **N:** 24 **Age, mean±SD (range):** 16.3±1.1 **Males %:** 79.2 **Caucasian %:** 87.5 **Diagnostic breakdown (n):** bipolar disorder (8), other psychoses (8; major depressive episode with psychotic features (2), psychosis NOS (2), schizoaffective disorder (2), schizophreniform	**Treatment duration:** 6 mo **Run-in phase:** Yes **Run-in phase duration:** 3–5 day **Permitted drugs:** adjunctive medications **Prohibited drugs:** antipsychotics **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 9.7±6.6 **Concurrent treatments:** anticholinergics (8), antidepressants (10), antiepileptics (7), benzodiazepines (17), β-blockers (1), lithium (2) **GROUP 2** **Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 532.8±459.6 **Concurrent treatments:** analgesics (2), anticholinergics (3), antidepressants (8), antiepileptics (7), benzodiazepines (14), β-blockers (2), cough medications (1), iron compouNRs (1), lithium (6), NSAIDs (1)	**Benefits:** CGAS, CGI-S, PANSS, SDQ, YMRS, Cognitive function, medication adherence **Harms:** UKU, BAS, SAS, Akathisia, behavioral issues, BMI, constipation, hypokinesia, orthostatic dizziness prolactin-related AE, SAE, sedation, tachycardia, total AE, weight change	Psychotic symptoms in adolescents were reduced with both olanzapine and quetiapine, but cognitive measures were not improved. Significantly more weight gain was observed in patients treated with olanzapine.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	quetiapine before enrolment	disorder (2)), schizophrenia (8) **Treatment naïve (n):** 15 **Inpatients (n):** all **First episode psychosis (n):** all **Comorbidities:** psychosis (all)			
Armenteros et al., 2007 [7] **Country:** USA **Condition category:** ADHD **Funding:** Industry **Risk of bias:** Medium (subjective), Medium (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV, C-DISC 4 **Inclusion criteria:** (1) 7–12 yr, (2) constant dose of stimulant medication in the past 3 wk, (3) 3 acts of aggression in the past wk, 2 of which had to be acts of physical aggression against other people, objects, or self, (4) Aggression Questionnaire Predatory-Affective index score ≤0, (5) CGI-S ≥4, (6) Full Scale IQ ≥75, (7) normal results at screening from physical examination and laboratory tests **Exclusion criteria:** (1)	**Enrolled:** 25 **Analyzed:** 25 **Completed:** 23 **GROUP 1** **N:** 12 **Age, mean±SD (range):** 7.3±3.7 **Males %:** 83.3 **Caucasian %:** 50 **Diagnostic breakdown (n):** ADHD + aggressive behavior (12) **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (0), ODD (13), conduct disorder (6), GAD (1), separation anxiety disorder (3) **GROUP 2** **N:** 13 **Age, mean±SD (range):** 8.8±3.1 **Males %:** 92.3 **Caucasian %:** 46 **Diagnostic breakdown (n):** ADHD + aggressive behavior (13) **Treatment naïve (n):** 0 **Inpatients (n):** NR	**Treatment duration:** 4 wk **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** current psychostimulants **Prohibited drugs:** all medications other than current psychostimulants **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.1±0.6 mg/day **Concurrent treatments:** all groups: methylphenidate (15), mixed salts amphetamine (10) **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1±0.5 mg/day **Concurrent treatments:** see group 1	**Benefits:** CGI-I, CGI-S Medication adherence, response (CAS-P, CAS-T, CGI-I) **Harms:** Behavioral issues, BMI, somnolence, total AE, WAE, weight change	Compared to placebo, risperidone was modestly effective in combination with psychostimulants for treatment-resistant agression in ADHD.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	substance use disorder, (2) unstable medical or neurological illness, (3) history of intolerance or failure to respond to an adequate trial of risperidone, (4) suicidal or homicidal	**First episode psychosis (n):** NR **Comorbidities:** see group1			
Bastiaens et al., 2009 [96] **Country:** USA **Condition category:** Mixed conditions (BP, Schizophrenia, MDD, ASD) **Funding:** Internal funding **Newcastle-Ottawa Scale:** 6/8 stars	**Recruitment dates:** Dec 2004 to Sep 2005 **Study design:** Retrospective cohort **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV, Mini International Neuropsychiatric Interview for Children and Adolescents, Child/Adolescent Symptom Inventory **Inclusion criteria:** (1) 6–18 yr, (2) clinically significant aggressive behavior **Exclusion criteria:** NR	**Enrolled:** 46 **Analyzed:** 34 **Completed:** 34 **GROUP 1** **N:** 24 **Age, mean±SD (range):** 11.7±2.4 **Males %:** 83 **Caucasian %:** NR **Diagnostic breakdown (n):** bipolar disorder (6), CD (8), depressive disorder (0), mood disorder NOS (6), PDD (0), psychotic disorder (4) **Treatment naïve (n):** 18 **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 2** **N:** 22 **Age, mean±SD (range):** 12.1±2.9 **Males %:** 91 **Caucasian %:** NR **Diagnostic breakdown (n):** bipolar disorder (6), CD (6), depressive disorder (6), mood disorder NOS (2), PDD (2), psychotic disorder (0)	**Treatment duration:** 8.7 wk **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** stable doses of concomitant medications **Prohibited drugs:** NR **GROUP 1** **Drug name:** Aripiprazole **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 4.5±2.3 **Concurrent treatments:** atomoxetine (8), stimulants (2) **GROUP 2** **Drug name:** Ziprasidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 42.9±18 **Concurrent treatments:** atomoxetine (6), stimulants (8)	**Benefits:** NA **Harms:** Behavioral issues, EPS, sedation, WAE, weight change	The two medications appeared to be tolerated well: the most common reported side effect was sedation. Excessive sedation was responsible for all documented disruptions in treatment. Ziprasidone resulted in three times more frequent discontinuations, compared to Aripiprazole.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Treatment naïve (n): 16 **Inpatients (n):** NR **First episode psychosis (n):** NR			
Berger et al., 2008[8] **Country:** Australia **Condition category:** Schizophrenia and related **Funding:** Industry, Academic **Risk of bias:** Low (subjective), Low (objective)	**Recruitment dates:** July 2003 to Jan 2006 **Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV, SCID-I/P **Inclusion criteria:** (1) 15–25 yr, (2) first episode psychosis, (3) ≥1 of the following symptoms, present daily for ≥1 wk according to BPRS: somatic concerns, guilt, suspiciousness, hallucinations, unusual thought content, bizarre behavior, and/or conceptual disorganization **Exclusion criteria:** (1) previous treatment with antipsychotic medication (>1 wk), (2) presence of concurrent manic syndrome, MR (IQ<70), organic disorders presenting with a psychotic syndrome, epilepsy, (3) clinically significant	**Enrolled:** 141 **Analyzed:** 126 **Completed:** 126 **GROUP 1** **N:** 69 **Age, mean±SD (range):** 19.7±2.6 (15–24) **Males %:** 71 **Caucasian %:** NR **Treatment naïve (n):** 22 **Inpatients (n):** NR **First episode psychosis (n):** all **Comorbidities:** MR (0), psychosis (all), SA (28) **GROUP 2** **N:** 72 **Age, mean±SD (range):** 19±2.9 (15–24) **Males %:** 64.1 **Caucasian %:** NR **Treatment naïve (n):** 25 **Inpatients (n):** NR **First episode psychosis (n):** all **Comorbidities:** MR (0), psychosis (all), SA (30)	**Treatment duration:** 4 wk **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** anticholinergics, benzodiazepines, sertraline (50–200 mg/day), zopiclone, zolpidem **Prohibited drugs:** antipsychotics **GROUP 1** **Drug name:** Quetiapine (low) **Dosing variability:** fixed **Target dose (mg/day):** 200 **Daily dose (mg/day), mean±SD (range):** 200 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Quetiapine (high) **Dosing variability:** fixed **Target dose (mg/day):** 400 **Daily dose (mg/day), mean±SD (range):** 400 **Concurrent treatments:** NR	**Benefits:** BPRS, CGI-S, GAF, SANS, SOFAS, YMRS, health care system utilization, legal interaction, medication adherence, response, suicide **Harms:** UKU, Blood pressure, EPS, sedation, sexual dysfunction, somnolence, WAE, weight change	Quetiapine was safe and well-tolerated in acutely ill drug naïve first-episode psychosis patients.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	physical illness, (4) history of brain surgery or brain infarct, (5) concomitant medications that prolong the QT interval, (6) 20% deviation from normal-range laboratory values at baseline, (7) participation in any other studies involving investigational or marketed products concomitantly or within 30 days (8) having donated blood or blood products within the past 4 wk, (9) pregnant or lactating women, or women of childbearing potential not using an acceptable method of contraception				
Biederman et al., 2005 [9] **Country:** USA **Condition category:** Bipolar (manic, hypomanic, mixed) **Funding:** Government, Academic **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV, K-SADS **Inclusion criteria:** (1) 4–6 yr, (2) DSM-IV bipolar I or II disorder or bipolar disorder NOS with current manic, hypomanic , or	**Enrolled:** 31 **Analyzed:** 31 **Completed:** 24 **GROUP 1** **N:** 15 **Age, mean±SD (range):** 5.0±0.8 **Males %:** 67 **Caucasian %:** 100 **Diagnostic breakdown (n):** major depression (11), mania (all) **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** ADHD	**Treatment duration:** 8 wk **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** benztropine mesylate (max 2 mg/day), lorazepam (≤2 mg/day) **Prohibited drugs:** antidepressants, antimanic or mood-stabilizing medications **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 6.3±2.3 (1.3–10)	**Benefits:** BPRS, CDRS, YMRS, Response **Harms:** Behavioral issues, blood pressure, cardiovascular AE, dermatologic AE, glucose, lipid profile, neurologic AE, prolactin, pulse, sedation, weight change	Rispiradone and olanzapine showed reduction of symptoms of mania in preschool children with bipolar disorder.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	mixed symptoms (with or without psychotic features), (3) YMRS score >15 **Exclusion criteria:** (1) any serious, unstable medical illness, (2) history of treatment with both study medications	(15), DBD (8) **GROUP 2** **N:** 16 **Age, mean±SD (range):** 5.3±0.8 **Males %:** 75 **Caucasian %:** 94 **Diagnostic breakdown (n):** major Depression (11), mania (all) **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** ADHD (14), DBD (5)	**Concurrent treatments:** all groups: benztropine (1), lorazepam (1) **GROUP 2** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.4±0.5 (0.3–2.0) **Concurrent treatments:** see group 1		
Bobo et al., 2013 [97] **Country:** USA **Condition category:** Mixed conditions **Funding:** Non-industry **Newcastle-Ottawa Scale:** 8/8 stars	**Recruitment dates:** Jan 1996 to Dec 2007 **Study design:** Retrospective **Setting:** NR **Diagnostic criteria:** NR **Inclusion criteria:** (1) adequate enrollment and health care utilization in the past year to ensure availability of data for study variables, (2) no evidence of life-threatening illness or institutional residence, (3) no evidence of diabetes, (4) no evidence of pregnancy	**Enrolled:** NA **Analyzed:** 43287 **Completed:** 43287 **GROUP 1** **N:** 28858 **Age, mean±SD (range):** 14.5 yr **Males %:** 56.0 **Caucasian %:** 72.8 **Diagnostic breakdown (n):** BP (5281), depression (5569), other mood disorder (9609), ADHD (11225), CD (7301), anxiety (5944), alcohol use (894), other substance use (2568) **Treatment naïve (n):** 0 **Inpatients (n):** 4184 **First episode psychosis (n):** NR **Comorbidities:** Menstruation absent or	**Treatment duration:** ≥1 yr **Run-in phase:** Yes **Run-in phase duration:** 365 d **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Antipsychotic users **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** [starting dose, median(IQ range)] 67(33-100)mg of chlorpromazine equivalents **Concurrent treatments:** Li (1212), valproate (2741), lamotrigine, carbamazepine, oxcarbazepine (2539), other mood stabilizer (519), SSRI (13563), heterocyclic antidepressant (4299), psychostimulant (9840), α-agonist (4213), benzodiazepine (3578)	**Benefits:** NA **Harms:** Type 2 diabetes mellitus	In the study cohort (6 to24 yr), those recently initiating an antipsychotic medication had a 3-fold greater risk of newly diagnosed type 2 diabetes than did propensity score–matched controls. Risk was elevated during the first year of antipsychotic use, increased with increasing cumulative dose, and was present for children <18 yr.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	(gestational diabetes might be misdiagnosed) or polycystic ovarian syndrome (treated with oral hypoglycemics), (5) cohort members could not have been in the hospital in the past month because changes in the medication regimen cannot be identified until up to 30 days following hospital discharge, (6) could have non-qualifying use of antipsychotics in the 90 days preceding the qualifying prescription but had to have a prior period of 365 days free of antipsychotic use, (7) cohort was restricted to recent users to include cases of diabetes that occurred early in therapy and to ensure that baseline covariateswere unaffected by chronic antipsychotic effects **Exclusion criteria:** (1) patientswithdiagnosed conditions for which antipsychotics generally are the only recommended treat-	infrequent (1096), menstruation disorder (1414), diagnosed obesity (1096), metabolic disorder (606), blood chemistry panel with glucose (6608), hypertension (750), other diagnosed cardiovascular disease (1298) **GROUP 2** **N:** 14429 **Age, mean±SD (range):** 14.5 yr **Males %:** 55.9 **Caucasian %:** 73.5 **Diagnostic breakdown (n):** BP (2654), depression (2813), other mood disorder (4689), ADHD (5526), CD (3592), anxiety (2871), alcohol use (476), other substance use (1341) **Treatment naïve (n):** NR **Inpatients (n):** 1991 **First episode psychosis (n):** NR **Comorbidities:** Menstruation absent or infrequent (533), menstruation disorder (72), diagnosed obesity (562), metabolic disorder (303), blood chemistry panel with glucose (3246), hypertension (360), other diagnosed cardiovascular disease (606)	**GROUP 2** **Drug name:** Controls **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** Li (591), valproate (1341), lamotrigine, carbamazepine, oxcarbazepine (1298), other mood stabilizer (259), SSRI (6723), heterocyclic antidepressant (2063), psychostimulant (4862), α-agonist (2048), benzodiazepine (1818)		

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	ment (eg. schizophrenia or related psychoses, organic psychoses, autism, mental retardation, Tourette syndrome, or other tic disorders), (2) patients prescribed clozapine or long-acting injectable preparations, usually indicators of schizophrenia or related psychoses, as well as those with parenterally administered drugs, typically given for transient agitation.				
Bruggeman et al., 2001 [10] **Country:** Belgium, Netherlands, South Africa **Condition category:** Tic disorders **Funding:** Industry **Risk of bias:** NA (subjective), Medium (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-III-TR **Inclusion criteria:** (1) 10–65 yr, (2) primary dx of Tourette syndrome (DSM-III-R), (3) ≥3 on TSSS and CGI-S **Exclusion criteria:** NR	**Enrolled:** 50 **Analyzed:** 50 **Completed:** 41 **GROUP 1** **N:** 24 **Age, mean±SD (range):** NR (11–45) **Males %:** 87.5 **Caucasian %:** NR **Diagnostic breakdown (n):** Tourette syndrome (24) **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** ADHD (1), GAD (2), OCD (14) **GROUP 2** **N:** 26 **Age, mean±SD (range):**	**Treatment duration:** 2.8 mo **Run-in phase:** Yes **Run-in phase duration:** 2–5 wk **Permitted drugs:** antiparkinsonian medication and benzodiazepines (discontinued during washout period, limited during treatment) **Prohibited drugs:** antiparkinsonian medication and benzodiazepines (discontinued during washout period, limited during treatment), psychotropics (within 2 wk prior to and during study) **GROUP 1** **Drug name:** Pimozide **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 2. 9 (1–6) **Concurrent treatments:** NR	**Benefits:** NR **Harms:** Weight	Risperidone and pimozide were efficacious and well tolerated in patients with Tourette syndrome, but risperidone had a more favorable efficacy and tolerability profile.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		NR (11–50) **Males %:** 88.5 **Caucasian %:** NR **Diagnostic breakdown (n):** Tourette syndrome (26) **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** ADHD (1), GAD (1), OCD (9)	**GROUP 2** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 3.8 (0.5–6) **Concurrent treatments:** NR		
Buchsbaum et al., 2007 [11] **Country:** USA **Condition category:** Schizophrenia and related **Funding:** Industry, government **Risk of bias:** Medium (subjective), NA (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Outpatient **Diagnostic criteria:** DSM-IV using CASH (at least Psychosis NOS) **Inclusion criteria:** (1) 13-21 yr, (2) never previously medicated **Exclusion criteria:** NR	**Enrolled:** 30 **Analyzed:** 22 **Completed:** 22 **GROUP 1** **N:** 10 **Age, mean±SD (range):** both groups: 16.2±2.0 **Males %:** both groups: 52 **Caucasian %:** NR **Treatment naïve (n):** 10 **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 2** **N:** 12 **Age, mean±SD (range):** see group 1 **Males %:** see group 1 **Caucasian %:** NR **Treatment naïve (n):** 12 **Inpatients (n):** NR **First episode psychosis (n):** NR	**Treatment duration:** 8-9 wks **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Haloperidol **Dosing variability:** variable **Target dose (mg/day):** up to 20mg/day **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 2** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** up to 20mg/day **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	**Benefits:** BPRS **Harms:** NR	Both patients treated with olanzapine and haloperidol improved significantly from baseline to week 8 on the BPRS (positive, negative, and total symptom scores).
Buitelaar et al., 2001 [12] **Country:**	**Recruitment dates:** NR **Study design:** RCT	**Enrolled:** 38 **Analyzed:** 38 **Completed:** 35	**Treatment duration:** 6 wk **Run-in phase:** Yes **Run-in phase duration:** 2 wk	**Benefits:** ABC, CGI-S, OAS-M Medication adherence	Risperidone may be effective for severe aggression in adolescents with

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Netherlands **Condition category:** ADHD **Funding:** Industry **Risk of bias:** Medium (subjective), Medium (objective)	(parallel) **Setting:** Inpatient **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) overt aggressive behavior persisted during hospitalization (modified OAS score ≥1), (2) failure to respond to behavioral treatment approaches, (3) clinical indication for drug treatment, (4) 12–18 yr, (5) principal dx of CD, ODD, or ADHD according to DSM-IV, (6) full-scale IQ 60–90 (WISC-R) **Exclusion criteria:** (1) neurologic, cardiac, pulmonary, or hepatic diseases, (2) primary mood disorders, schizophrenia or other active psychosis, or suicidality, (3) comorbid substance abuse disorder (DSM-IV), (4) pregnant or use of inadequate contraception, (5) major change in treatment strategy expected, (6) not feasible to discontinue current psychotropic medication	**GROUP 1** **N:** 19 **Age, mean±SD (range):** 14.0±1.5 (11–18) **Males %:** 89.5 **Caucasian %:** NR **Diagnostic breakdown (n):** CD (14), DBD NOS (1), ODD (4) **Treatment naïve (n):** 13 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (14), MR (6) **GROUP 2** **N:** 19 **Age, mean±SD (range):** 13.7±2 (11–18) **Males %:** 84.2 **Caucasian %:** NR **Diagnostic breakdown (n):** CD (16), DBD NOS (1), ODD (2) **Treatment naïve (n):** 13 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (12), anxiety disorder (3), MR (8)	**Permitted drugs:** biperidine, medication for somatic illness, oxazepam **Prohibited drugs:** psychotropics **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 2.9 (1.5–4) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	**Harms:** Akathisia, dyskinesia, dystonia, ECG changes, fatigue, oculogyric crisis, parkinsonism, prolactin, prolactin-related AE, SAE, somnolence, total AE, weight change, ESRS	disruptive behavior disorders and subaverage intelligence.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Calarge et al., 2014 [98] **Country:** USA **Condition category:** Mixed **Funding:** Non-industry **Newcastle-Ottawa Scale:** 5/8 stars	**Recruitment dates:** NR **Study design:** Prospective **Setting:** NR **Diagnostic criteria:** DSM-IV-TR, DISC-IV **Inclusion criteria:** (1) 7-7 yr, (2) treated with risperidone ≥6 mo, irrespective of primary diagnosis **Exclusion criteria:** (1) Participants with neurological or medical conditions that could confound the cardiometabolic assessments (e.g., seizure disorder, hypothyroidism, dyslipidemia, diabetes), (2) pregnant females, (3) those receiving hormonal contraception	**Enrolled:** 108 **Analyzed:** 101 **Completed:** 101 **GROUP 1** **N:** 74 **Age, mean±SD (range):** 13.3±2.7 yr **Males %:** 95 **Caucasian %:** 80 **Diagnostic breakdown (n):** DBD (68), ADHD (65), anxiety disorder (23), depressive disorder (3), ASD (12), tic disorder (17) **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 9 **Age, mean±SD (range):** 12.3±2.6 yr **Males %:** 89 **Caucasian %:** 67 **Diagnostic breakdown (n):** DBD (7), ADHD (7), anxiety disorder (3), depressive disorder (0), ASD (2), tic disorder (3) **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 3** **N:** 18 **Age, mean±SD (range):** 13.1±2.3 yr	**Treatment duration:** 6 mo, followed-up after 1.5 yr **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone Continued **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** (mg/kg/d) 0.03±0.02 **Concurrent treatments:** Psychostimulants (59), α_2-agonists (25), antidepressants (43), mood stabilizers (6) **GROUP 2** **Drug name:** SGA Continued **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** Psychostimulants (5), α_2-agonists (6), antidepressants (8), mood stabilizers (0) **GROUP 3** **Drug name:** SGA Discontinued **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** Psychostimulants (11), α_2-agonists (5), antidepressants (20), mood stabilizers (2)	**Benefits:** NA **Harms:** Weight (BMI-z), lipid values, glucose, insulin, blood pressure (systolic/ diastolic), prolactin	Discontinuation of risperidone is associated with largely spontaneous resolution of the excessive weight and a favorable change in cardiometabolic parameters.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Males %: 89 **Caucasian %:** 94 **Diagnostic breakdown (n):** DBD (14), ADHD (17), anxiety disorder (5), depressive disorder (2), ASD (5), tic disorder (5) **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR			
Castro-Fornieles et al., 2008 [99] **Country:** Spain **Condition category:** Schizophrenia and related **Funding:** Government **Newcastle-Ottawa Scale:** 6/8 stars	**Recruitment dates:** NR **Study design:** Prospective cohort **Setting:** Inpatient (84% at recruitment) and outpatient **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) 7 to 17 yr, (2) psychotic episode less than 6 mo duration **Exclusion criteria:** (1) ASD, PTSD, SUD and other Axis I associated with psychosis, (2) MR and PDD	**Enrolled:** 110 **Analyzed:** 60 (only those remaining on same medication) **Completed:** 60 **All patients:** 15.5±1.8; Males 67%; White: 86%; 49% drug naive **GROUP 1** **N:** 31 **Age, mean±SD (range):** 15.1±2.1 **Males %:** 68 **Caucasian %: NR** **Treatment naïve (n):** NR **Inpatients (n): NR** **First episode psychosis (n):** 31 **GROUP 2** **N:** 15 **Age, mean±SD (range):** 16.4±1.1 **Males %:** 67 **Caucasian %:** NR **Treatment naïve (n):** NR	**Treatment duration:** 24 mo **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone **Dosing variability: variable** **Target dose (mg/day): NR** **Daily dose (mg/day), mean±SD (range):** 2.8±1.2mg/day **Concurrent treatments:** NR **GROUP 2** **Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 626.8±526 mg/day **Concurrent treatments:** NR **GROUP 3** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD	**Benefits:** PANSS, CGI, GAF **Harms:** Weight, BMI, UKU, neurological AEs	Using the baseline score as covariate, there were no statistically significant differences between the three antipsychotics in the improvement achieved on any scale. Clinicians seem to prefer quetiapine or olanzapine to risperidone when there are marked affective symptoms.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Inpatients (n): NR **First episode psychosis (n):** 15 **GROUP 3** **N:** 14 **Age, mean±SD (range):** 15.7±1.2 **Males %:** 71 **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** 14	**(range):** 11.7±7.0 mg/day **Concurrent treatments:** NR		
Cianchetti et al., 2011 [100] **Country:** Italy **Condition category:** Schizophrenia and related **Funding:** NR **Newcastle-Ottawa Scale:** 5/8 stars	**Recruitment dates:** 1990 to 2005 **Study design:** Cohort study **Setting:** Inpatient (at recruitment) and outpatient **Diagnostic criteria:** DSM-IV **Inclusion criteria:** schizophrenia or schizoaffective disorder **Exclusion criteria:** (1) concomitant axis I disorder, (2) IQ less than 70, (3) neurological disorders and previous commotive head trauma	**Enrolled:** 58 **Analyzed:** 47 **Completed:** 47 **Whole cohort:** **Age:** 15.5 (range 10-17) **Males:** 45% **Caucasian**: 100%	**Treatment duration:** see below: 3 to 11 yrs **Run-in phase:** **Run-in phase duration:** **Permitted drugs:** mood stabilizers, anti-EPS (for haloperidol and high dose risperidone) **Prohibited drugs:** NR All patients treated per protocol, with analysis based on drugs used (haloperidol, risperidone, olanzapine, clozapine, quetiapine, aripiprazole; latter two had too few patients to compare) Haloperidol: (29) mean months treatment 9.4±14.3 Risperidone: (33) mean months of treatment 19.6±17.9 Olanzapine: (12) mean months of treatment 11.7±9.2 Clozapine: (28) mean months of treatment 31.5±916.3	**Benefits:** PANSS, CGI-I, CGI-EI, C-GAS, response **Harms:** EPS, weight, ECG, glucose, liver function tests, discontinuations, neutropenia, suicide	In the long-term, clozapine is more effective than haloperidol, risperidone and olanzapine. Despite a relevant incidence of adverse effects, clozapine seems to have unique effectiveness in treating children and adolescents with early-onset schizophrenic disorders.
Connor et al., 2008 [13]	**Recruitment dates:** Nov 2003 to May 2005	**Enrolled:** 19 **Analyzed:** 19	**Treatment duration:** 6 wk **Run-in phase:** Yes	**Benefits:** CGI-I, CGI-S, Conner PRS, OAS	Quetiapine may be efficacious in the

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Completed: 11	**Run-in phase duration:** 1–4 wk	Quality of life (Q-LES-Q), school attendance	treatment of CD, but further research is required.
Country: USA	**Study design:** RCT (parallel)	**GROUP 1**	**Permitted drugs:** benztropine		
Condition category: ADHD	**Setting:** Outpatient/community	**N:** 9 **Age, mean±SD (range):** 13.1±1.2 yr	**Prohibited drugs:** psychotropics, rescue medications for aggression	**Harms:** Akathisia, Behavioral issues, ECG changes, EPS, prolactin, pulse, SAE, sedation, severity of AE, WAE, weight change, AIMS	
Funding: Industry	**Diagnostic criteria:** K-SADS-E	**Males %:** 78% **Caucasian %:** 78% **Diagnostic breakdown:** CD with moderate to severe aggression (9)	**GROUP 1** **Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** 200 **Daily dose (mg/day), mean±SD (range):** 294±78 (200–600) **Concurrent treatments:** benztropine (0)		
Risk of bias: High (subjective), High (objective)	**Inclusion criteria:** (1) 12–17 yr, (2) primary psychiatric dx of CD, (3) moderate to severe aggression (OAS score ≥25), (4) at least moderate severity of symptoms (CGI-S score ≥4)	**Treatment naïve (n):** 2 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (8), DBD (8), depression (1), dysthymia (2), GAD (3), MR (0), OCD (2), panic disorder (1), psychosis (0), PTSD (2), SA (1), separation anxiety (2), social phobia (2)	**GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** 200 **Daily dose (mg/day), mean±SD (range):** 530±245 **Concurrent treatments:** benztropine (0)		
	Exclusion criteria: (1) comorbid schizophrenia, schizoaffective disorder, psychotic disorder NOS, bipolar disorder, psychotic depression, or bipolar disorder NOS, (2) alcohol or substance abuse or dependence within 3 mo, (3) significantly subaverage IQ, (4) current or past history of leticular abnormality or juvenile cataracts, (5) seizure disorder, (6) concurrent administration of any psychoactive medication, (7)	**GROUP 2** **N:** 10 **Age, mean±SD (range):** 15±1.4 yr **Males %:** 70% **Caucasian %:** 70% **Diagnostic breakdown:** CD with moderate to severe aggression (10) **Treatment naïve (n):** 1 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (7), DBD (10), depression (3), dysthymia (3), GAD (0), MR (0), OCD (1), panic disorder (0),			

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	pregnant or lactating females, (8) women of childbearing potential not using a medically accepted means of birth control, (9) unstable medical disease	psychosis (0), PTSD (1) SA (5), separation anxiety (1), social phobia (1)			
Correll et al., 2009 [101] **Country:** USA **Condition category:** Mixed conditions (bipolar, ADHD, ASD, schizophrenia-related) **Funding:** Government, Academic **Newcastle-Ottawa Scale:** 8/8 stars	**Recruitment dates:** Dec 2001 to Sep 2007 **Study design:** Prospective cohort **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV, chart review, discussion with treating clinician, clinical interview **Inclusion criteria:** (1) 4–19 yr, (2) <1 wk lifetime antipsychotic treatment, (3) psychiatric illness prompting antipsychotic medication initiation, (4) consent, (5) baseline anthropometric and biochemical assessments obtained within 7 day of antipsychotic medication initiation **Exclusion criteria:** (1) treatment with >1	**Enrolled:** 312 **Analyzed:** 257 **Completed:** 192 **GROUP 1** **N:** 47 **Age, mean±SD (range):** 13.4±3.1 (7–19.7) **Males %:** 56.1 **Caucasian %:** NR **Diagnostic breakdown (n):** disruptive or aggressive behavior spectrum disorder (9: ASD (4), ODD, CD, IED, ICD (5)), mood disorder spectrum (11: bipolar (3), MDD (10), NOS (5)), schizophrenia spectrum (14: psychosis NOS (11), schizophrenia/ schizoaffective disorder (3)) **Treatment naïve (n):** all **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 52 **Age, mean±SD (range):** 14.7±3.2 (6.6–18.6) **Males %:** 64.4	**Treatment duration:** 2.8 mo **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** co-medications as necessary **Prohibited drugs:** co-medications as necessary **GROUP 1** **Drug name:** Aripriprazole **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** anticholinergics (2), antidepressants (13), anxiolytics or hypnotics (1), mood stabilizers (6), none (16), psychostimulants (5), psychotropics (4) **GROUP 2** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** anticholinergics (0), antidepressants (10), anxiolytics or hypnotics (3), mood stabilizers (18), none (14), psychostimulants (4), psychotropics	**Benefits:** NR **Harms:** Fat mass, glucose, insulin resistance, lipid profile, metabolic syndrome, waist circumference, WAE, weight change	First-time SGA medication use was associated with significant weight gain and variable metabolic changes for each medication.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	antipsychotic agent, (2) active or past eating disorder, (3) biochemical evidence of thyroid dysfunction, (4) acute medical disorders, (5) pregnancy or breastfeeding, (6) wards of the state, (7) leaving the catchment area within 4 wk	**Caucasian %:** NR **Diagnostic breakdown (n):** disruptive or aggressive behavior spectrum disorder (9: ASD (2), ODD, CD, IED, ICD (7)), mood disorder spectrum (16: bipolar (9), MDD (8), NOS (4)), schizophrenia spectrum (14: psychosis NOS (5), schizophrenia/ schizoaffective disorder (9)) **Treatment naïve (n):** all **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 3** **N:** 45 **Age, mean±SD (range):** 14±3.1 (6.1–19.4) **Males %:** 36.1 **Caucasian %:** NR **Diagnostic breakdown (n):** disruptive or aggressive behavior spectrum disorder (6: ASD (2), ODD, CD, IED, ICD (4)), mood disorder spectrum (9: bipolar (10), MDD (8), NOS (6)), schizophrenia spectrum (6: psychosis NOS (4), schizophrenia/ schizoaffective disorder (2)) **Treatment naïve (n):** all **Inpatients (n):** NR **First episode psychosis**	(1) **GROUP 3** **Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** anticholinergics (2), antidepressants (10), anxiolytics or hypnotics (1), mood stabilizers (15), none (8), psychostimulants (4), psychotropics (1) **GROUP 4** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** anticholinergics (18), antidepressants (43), anxiolytics or hypnotics (13), mood stabilizers (32), none (32), psychostimulants (26), psychotropics (9)		

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		(n): NR **Comorbidities:** NR **GROUP 4** **N:** 168 **Age, mean±SD (range):** 13.6±4 (4.3–19.9) **Males %:** 62.2 **Caucasian %:** NR **Diagnostic breakdown (n):** disruptive or aggressive behavior spectrum disorder (34: ASD (13), ODD, CD, IED, ICD (21)), mood disorder spectrum (55: bipolar (17), MDD (19), NOS (19)), schizophrenia spectrum (46: psychosis NOS (33), schizophrenia/ schizoaffective disorder (13)) **Treatment naïve (n):** all **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR			
Crocq et al., 2007 [14] **Country:** France **Condition category:** Schizophrenia and related **Funding:** NR **Risk of bias:** NA (subjective), High	**Recruitment dates:** NR **Study design:** NRCT (parallel) **Setting:** Inpatient **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) hospitalized adolescents with	**Enrolled:** NR **Analyzed:** 52 **Completed:** NR **GROUP 1** **N:** NR **Age, mean±SD (range):** 16.5±1.7 **Males %:** 31.3 **Caucasian %:** all **Treatment naïve (n):** NR **Inpatients (n):** all **First episode psychosis (n):** NR	**Treatment duration:** 2.8 mo **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Olanzapine (oral disintegrating tablet) **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD**	**Benefits:** NR **Harms:** BMI, weight	Significantly greater increases in weight and BMI were found for olanzapine SOT compared to olanzapine ODT, as well as for olanzapine ODT compared to risperidone.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
(objective)	schizophreniform disorder **Exclusion criteria:** NR	**GROUP 2** **N:** NR **Age, mean±SD (range):** 17±1.3 **Males %:** 60 **Caucasian %:** all **Treatment naïve (n):** NR **Inpatients (n):** all **First episode psychosis (n):** NR **GROUP 3** **N:** NR **Age, mean±SD (range):** 15.2±1.4 **Males %:** 57.7 **Caucasian %:** all **Treatment naïve (n):** NR **Inpatients (n):** all **First episode psychosis (n):** NR	**(range):** 16.6±4.4 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Olanzapine (standard oral tablet) **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 18±4.2 **Concurrent treatments:** NR **GROUP 3** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 2. 8±1.2 **Concurrent treatments:** NR		
Cuerda et al., 2011 [102] **Country:** Spain **Condition category:** Mixed conditions **Funding:** Non-industry **Newcastle-Ottawa Scale:** 6/8 stars	**Recruitment dates:** Feb 2005-Sept 2007 **Study design:** Prospective **Setting:** NR **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) 11-18 yr, (2) mental disorder requiring treatment with antipsychotics, (3) antipsychotic naïve patients or quasi-naïve (<72hr of exposure to antipsychotics), (4)	**Enrolled:** 61 **Analyzed:** 46 **Completed:** 16 **GROUP 1** **N:** 18 **Age, mean±SD (range):** 16.1±1.9 yr **Males %:** 83.3 **Caucasian %:** 72.2 **Diagnostic breakdown (n):** BP (1), brief psychosis/schizophria disorder (4), conduct disorder (3), depression with psychotic symptoms (2), OCD (0), psychosis NOS (6), schizophrenia (2), scholar phobia (0), depression (0), intellectual	**Treatment duration:** 1 yr **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 2** **Drug name:** Olanzapine **Dosing variability:** NR **Target dose (mg/day):** NR	**Benefits:** NR **Harms:** Weight, BMI, lipid values, glucose, insulin, prolactin	Hypometabolism may explain weight gain in patients taking SGAs. Lifestyle recommendations involving reduced calorie intake and increased physical activity should be prescribed in all patients starting these treatments.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	written informed consent signed by parents or legal representatives and patients after the syudy was explained **Exclusion criteria:** (1) Concomitant use of medications that can influence body weight (corticosterioids, valproic acid or lithium), (2) presence of diabetes mellitus and severe dyslipidemia, (3) if a second antipsychotic was prescribed, (4) if treatment was changed or withdrawn during follow up, (5) if adherence was poor	disability (0), personality disorder (0) **Treatment naïve (n):** 10 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 12 **Age, mean±SD (range):** 16.1±1.3 yr **Males %:** 66.7 **Caucasian %:** 91.7 **Diagnostic breakdown (n):** BP (4), brief psychosis/schizophria disorder (2), conduct disorder (1), depression with psychotic symptoms (0), OCD (1), psychosis NOS (2), schizophrenia (1), scholar phobia (1), depression (0), intellectual disability (0), personality disorder (0) **Treatment naïve (n):** 5 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 3** **N:** 16 **Age, mean±SD (range):** 16.6±0.7 yr **Males %:** 62.5 **Caucasian %:** 81.3 **Diagnostic breakdown (n):** BP (2), brief psychosis/schizophria disorder (4), conduct	**Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 3** **Drug name:** Quetiapine **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR		

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		disorder (0), depression with psychotic symptoms (1), OCD (2), psychosis NOS (3), schizophrenia (1), scholar phobia (0), depression (1), intellectual disability (1), personality disorder (1) **Treatment naïve (n):** 5 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR			
de Haan et al., 2003 [15] **Country:** Netherlands **Condition category:** Schizophrenia and related **Funding:** Government **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) 17–28 yr, (2) DSM-IV criteria for schizophrenia, (3) admitted to the Adolescent Clinic **Exclusion criteria:** (1) neurological or endocrine disease, (2) MR, (3) use of adjunctive medications such as mood stabilizers or antidepressants, (4) history of treatment	**Enrolled:** 24 **Analyzed:** 19 **Completed:** 20 **GROUP 1** **N:** 12 **Age, mean±SD (range):** 21.0±2.8 (17–26) **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** 9 **Comorbidities:** MR (0) **GROUP 2** **N:** 12 **Age, mean±SD (range):** 21±2.3 (17–25) **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** 11 **Comorbidities:** MR (0)	**Treatment duration:** 6 wk **Run-in phase:** Yes **Run-in phase duration:** 1 wk **Permitted drugs:** oxazepam **Prohibited drugs:** antidepressants, antipsychotics, mood stabilizers **GROUP 1** **Drug name:** Haloperidol **Dosing variability:** fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 2.5 **Concurrent treatments:** oxazepam (6) **GROUP 2** **Drug name:** Olanzapine **Dosing variability: f**ixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 7.5 **Concurrent treatments:** oxazepam (5)	**Benefits:** CGI-I, PANSS, health related quality of life (Subjective Well-Being Under Neuroleptics scale), medication adherence **Harms:** BAS, SAS, akathisia, parkinsonism	Olanzapine showed no superior subjective response over haloperidol in patients with recent-onset schizophrenia.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	with clozapine, (5) history of unresponsiveness to haloperidol or olanzapine, (6) intramuscular antipsychotic treatment within the last yr				
DelBello et al., 2009 [18] **Country:** USA **Condition category:** Bipolar (depressive) **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** Mar 2006 to June 2007 **Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV-TR, WASH-U-KSADS **Inclusion criteria:** (1) 12–18 yr, (2) dx of bipolar I disorder, depressive episode, (3) screening and baseline CDRS-R score ≥40 **Exclusion criteria:** (1) substance use disorder (other than nicotine) within the previous 3 mo, (2) unstable medical or neurological illness, (3) history of intolerance or nonresponse to quetiapine monotherapy, (4) treatment with an antidepressant (other	**Enrolled:** 32 **Analyzed:** 32 **Completed:** 20 **GROUP 1** **N:** 17 **Age, mean±SD (range):** 16.0±2 **Males %:** 29 **Caucasian %:** 82 **Treatment naïve (n):** 12 **Inpatients (n):** 7 **First episode psychosis (n):** NR **Comorbidities:** ADHD (2), anxiety disorder (5), DBD (6), psychosis (2) **GROUP 2** **N:** 15 **Age, mean±SD (range):** 15±2 **Males %:** 33 **Caucasian %:** 80 **Treatment naïve (n):** 11 **Inpatients (n):** 8 **First episode psychosis (n):** NR **Comorbidities:** ADHD (2), anxiety disorder (3), DBD (2), psychosis (1)	**Treatment duration:** 8 wk **Run-in phase:** Yes **Run-in phase duration:** NR **Permitted drugs:** lorazepam (max 4 mg/day days 1–7, 2 mg/day days 8–14) **Prohibited drugs:** antidepressants (<3 day), anticonvulsants (<3 day), antipsychotics or atomoxetine (<3 day), fluoxetine (<4 wk), psychostimulant (<48 hr) **GROUP 1** **Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** 600 **Daily dose (mg/day), mean±SD (range):** 403±133 (300–600) **Concurrent treatments:** lorazepam (0) **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** 600 **Daily dose (mg/day), mean±SD (range):** 413±151 (300–600) **Concurrent treatments:** lorazepam (0)	**Benefits:** CDRS, CGI-BP, HAM-A, YMRS, response (response, remission, suicide attempt) **Harms:** Blood pressure, BMI, diabetes, EPS, glucose, LFT, lipid profile, mania, prolactin, pulse, SAE, sedation, tachycardia, WAE, weight change, EPS	Quetiapine monotherapy was no more effective in treating depression in adolescents with bipolar disorder than treatment with placebo.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	than fluoxetine), an anticonvulsant (other than valproate or carbamazepine), antipsychotic or atomoxetine within 3 day, fluoxetine within 4 wk, or a psychostimulant within 48 hr of baseline, (5) risk of suicide				
DelBello et al., 2008 [17] **Country:** USA **Condition category:** Bipolar & schizophrenia-related **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV-TR **Inclusion criteria:** (1) 10–17 yr, (2) bipolar I disorder (YMRS score ≥17), (3) schizophrenia-related disorder (BPRS-A score ≥35, with a score of ≥4 on at least one of: unusual thought content, hallucinations, suspiciousness, or conceptual disorganization), (4) BMI between 5th and 95th percentile **Exclusion criteria:** (1) currently on stable well-tolerated	**Enrolled:** 63 **Analyzed:** 63 **Completed:** 38 **GROUP 1** **N:** 23 **Age, mean±SD (range):** 13.2 (bipolar), 14.4 (schiz) **Males %:** 52 **Caucasian %:** NR **Diagnostic breakdown (n):** bipolar I (15), schizophrenia or schizoaffective disorder (8) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (0), SA (0) **GROUP 2** **N:** 40 **Age, mean±SD (range):** 13.8 (bipolar), 14.7 (schiz) **Males %:** 75 **Caucasian %:** NR **Diagnostic breakdown (n):** biploar I (31), schizophrenia or	**Treatment duration:** 3 wk **Run-in phase:** Yes **Run-in phase duration:** 24 hr **Permitted drugs:** benztropine and/or propranolol, lorazepam or similar benzodiazepine **Prohibited drugs:** antidepressants, mood stabilizers, stimulants **GROUP 1** **Drug name:** Ziprasidone (low) **Dosing variability:** fixed **Target dose (mg/day):** 80 **Daily dose (mg/day), mean±SD (range):** (20–80) **Concurrent treatments:** benztropine (3) **GROUP 2** **Drug name:** Ziprasidone (high) **Dosing variability:** fixed **Target dose (mg/day):** 160 **Daily dose (mg/day), mean±SD (range):** (40–160) **Concurrent treatments:** benztropine (4)	**Benefits:** YMRS, BPRS, CGI-S **Harms:** Akathisia, behavioral issues, dystonia, ECG changes, EPS (AIMS, SAS, BAS), fatigue, glucose, lipid profile, prolactin, SAE, sedation, somnolence, WAE, weight change	Neither low- nor high- dose ziprasidone was associated with unexpected tolerability findings, and a starting dose of 20 mg/d, titrated to 80–160 mg/d over 1–2 wk was optimal.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	treatment, (2) substance-induced psychotic disorder, (3) treatment with clozapine within 12 wk, (4) depot antipsychotic within 4 wk, (5) MAO-I within 2 wk, (6) imminent risk of suicide or homicide, (7) MR, (8) autism or other PDD, (8) pregnancy, breastfeeding, or unwillingness to use birth control, (9) serious unstable medical or neurologic illness, (10) any screening laboratory value that deviated significantly from reference range, (11) clinically significant hypokalemia or hypomagnesemia, (12) history of cardiac arryhthmias, conduction abnormalities, QTc prolongation, or genetic risk for prolonged QT syndrome, (13) psychoactive substance or alcohol abuse or dependence (other than nicotine or caffeine) within 1 mo (DSM-IV-TR)	schizoaffective disorder (9) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (0), SA (0)			
DelBello et al., 2002 [16]	**Recruitment dates:** May 2000 to May 2001	**Enrolled:** 30 **Analyzed:** 30 **Completed:** 22	**Treatment duration:** 6 wk **Run-in phase:** Yes **Run-in phase duration:** NR	**Benefits:** YMRS, Medication adherence, response	Quetiapine in combination with divalproate is more

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Country: USA **Condition category:** Bipolar (manic, mixed) **Funding:** Industry **Risk of bias:** Medium (subjective), Medium (objective)	**Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV, WASH-U-KSADS **Inclusion criteria:** (1) 12–18 yr, (2) DSM-IV criteria for bipolar I disorder, currently mixed or manic, (3) YMRS score ≥20 **Exclusion criteria:** (1) pregnant, (2) manic symptoms secondary to substance intoxication or withdrawal, (3) substance use disorder within the past 3 mo, (4) MR, (5) unstable medical or neurological disorder, cataracts, or clinically significant baseline laboratory abnormalities, (6) history of hypersensitivity, intolerance, or nonresponse to quetiapine or valproate, (7) treated with a depot neuroleptic within 3 mo, an antidepressant or antipsychotic within 1 wk (fluoxetine within	**GROUP 1** **N:** 15 **Age, mean±SD (range):** 14.1±2 **Males %:** 53 **Caucasian %:** 80 **Diagnostic breakdown (n):** mixed episode (10) **Treatment naïve (n):** NR **Inpatients (n):** all **First episode psychosis (n):** NR **Comorbidities:** ADHD (10), psychosis (7) **GROUP 2** **N:** 15 **Age, mean±SD (range):** 14.5±2 **Males %:** 53 **Caucasian %:** 87 **Diagnostic breakdown (n):** mixed episode (13) **Treatment naïve (n):** NR **Inpatients (n):** all **First episode psychosis (n):** NR **Comorbidities:** ADHD (8), psychosis (7)	**Permitted drugs:** lorazepam (≤2 mg/day for first 14 day) **Prohibited drugs:** NR **GROUP 1** **Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** 450 **Daily dose (mg/day), mean±SD (range):** 432 **Concurrent treatments:** lorazepam (2) **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** lorazepam (3)	**Harms:** Blood cells, blood pressure, ECG changes, prolactin, SAE, sedation, thyroid function, WAE, weight change, EPS (AIMS, BAS, SAS)	effective for the treatment of adolescent bipolar mania than divalproate with placebo.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	1 mo), a benzodiazepine or psychostimulant within 72 hr, or other antiepileptic agents within 72 hr				
Ebert et al., 2014 [103] **Country:** Israel **Condition category:** Mixed conditions **Funding:** NR **Newcastle-Ottawa Scale:** 5/8 stars	**Recruitment dates:** 2011-2012 **Study design:** Retrospective **Setting:** Inpatient **Diagnostic criteria:** NR **Inclusion criteria:** NR **Exclusion criteria:** NR	**Enrolled:** 72 **Analyzed:** 56 **Completed:** 56 **GROUP 1** **N:** 32 **Age, mean±SD (range):** 9.6±1.6 yr **Males %:** 91.7 **Caucasian %:** NR **Diagnostic breakdown (n):** See below **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** Anemia (1), ichthyosis (1) **GROUP 2** **N:** 24 **Age, mean±SD (range):** 9.3±1.8 yr **Males %:** 87.5 **Caucasian %:** NR **Diagnostic breakdown (n):** See below **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** Epilepsy (1), central precocious puberty (1) **Overall diagnostic**	**Treatment duration:** mean 10-17 wk for groups **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Atypical antipsychotic treatment **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 2** **Drug name:** Control **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	**Benefits:** NR **Harms:** Weight, BMI, lipid values, fasting glucose, transaminases (ALT, AST)	Weight and metabolic monitoring is essential as supposedly weight neutral antipsychotics (aripiprazole, ziprasidone, and amisulpride) may not be weight neutral in youth, especially in antipsychotic-naïve youth.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		breakdown (n): Psychotic spectrum disorder (15), BP (4), DBD (29), ADHD (26), anxiety spectrum disorder (8), depression disorder (13), PDD (5), MR (3), OCD (1), adjustment disorder (2), ED (1), tic disorder (2)			
Findling et al., 2015b [29] **Country:** USA **Condition category:** Bipolar I (manic, mixed) **Funding:** Industry **Risk of bias:** Low (subjective), Low (objective)	**Recruitment dates:** Jul 2011 to Sept 2013 **Study design:** RCT (parallel) **Setting:** Outpatient **Diagnostic criteria:** DSM-IV-TR, K-SADS-PL **Inclusion criteria:** (1) Dx of bipolar I disorder acute manic or mixed episode with DSM-IV-TR and K-SADS-PL, (2) YMRS score ≥20, (3) CGI-BP overall ≥4, (4) guardian living with the child who was able to ensure adherence with treatment, outpatient visits, and study protocol **Exclusion criteria:** (1) Pervasive development disorder, schizophrenia, schizoaffective disorder,	**Enrolled:** 404 **Analyzed:** 403 **Completed:** 350 **GROUP 1** **N:** 104 **Age, mean±SD (range):** 13.7±2.1 yr **Males %:** 50 **Caucasian %:** 72.1 **Diagnostic breakdown (n):** Manic (40), mixed (64) **Treatment naïve (n):** 38 **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** ADHD (62) **GROUP 2** **N:** 99 **Age, mean±SD (range):** 13.8±2.0 yr **Males %:** 43.4 **Caucasian %:** 67.7 **Diagnostic breakdown (n):** Manic (43), mixed (56) **Treatment naïve (n):** 24 **Inpatients (n):** 0 **First episode psychosis**	**Treatment duration:** 3 wk **Run-in phase:** Yes **Run-in phase duration:** 2-14 d **Permitted drugs:** Chronic use medication such as hormonal birth control, common over-the-counter medications (i.e., nutritional supplements, pain relievers, antacids); short-acting benzodiazepines (e.g., lorazepam and equivalents) as needed or diazepam; use of psychostimulants and other ADHD medications, medications to treat extrapyramidal symptoms (EPS; e.g., anticholinergics, short-acting benzodiazepines). . **Prohibited drugs:** Antipsychotics, depot neuroleptics, benzodiazepines [except for lorazepam, up to 4 mg daily, or otherwise the equivalent dose of short-acting benzodiazepines that were clinically indicated], antidepressants, mood stabilizers, miscellaneous psychotropics, and herbal drugs/dietary supplements for depression, anxiety, or insomnia)	**Benefits:** YMRS, CGI-BP-S, CGAS, CDRS-R, response, suicidal ideation, attempted suicide, psychiatric disorders, worsening of mania, medication adherence **Harms:** Mortality, somnolence, EPS (ESRS), akathisia, dystonia, weight gain, BMI, ECG, lipid values, fasting insulin, glucose, prolactin, nausea, orthostatic hypotension related adverse events	All asenapine doses versus placebo were superior based on change in YMRS at day 21. Asenapin was generally well tolerated in patients aged 10 to 17years with bipolar I disorder in manic or mixed states. Increases in weight and fasting insulin were associated with asenapine.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	posttraumatic stress disorder, obsessive-compulsive disorder, psychosis due to a medical condition, (2) prohibited concomitant medication, (3) uncontrolled, unstable, clinically significant medical condition	**(n):** NR **Comorbidities:** ADHD (45) **GROUP 3** **N:** 99 **Age, mean±SD (range):** 13.9±2.1 yr **Males %:** 58.6 **Caucasian %:** 65.7 **Diagnostic breakdown (n):** Manic (44), mixed (55) **Treatment naïve (n):** 32 **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** ADHD (61) **GROUP 4** **N:** 101 **Age, mean±SD (range):** 13.7±2.0 yr **Males %:** 37.6 **Caucasian %:** 67.3 **Diagnostic breakdown (n):** Manic (44), mixed (57) **Treatment naïve (n):** 43 **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** ADHD (52)	**GROUP 1** **Drug name:** Asenapine (2.5 mg) **Dosing variability:** fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** Stimulant (29) **GROUP 2** **Drug name:** Asenapine (5 mg) **Dosing variability:** fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** Stimulant (22) **GROUP 3** **Drug name:** Asenapine (10 mg) **Dosing variability:** fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** Stimulant (25) **GROUP 4** **Drug name:** Placebo **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** Stimulant (20)		
Findling et al., 2015a [28] **Country:** USA (19 centers), international (60	**Recruitment dates:** April 2011 to April 2013 **Study design:** RCT (parallel)	**Enrolled:** 306 **Analyzed:** **Completed:** **GROUP 1** **N:** 106	**Treatment duration:** 8 wk **Run-in phase:** Yes **Run-in phase duration:** 3-10 day **Permitted drugs:** short-acting benzodiazepines (lorazepam 4mg or	**Benefits:** PANSS, CGI-S, response **Harms:** EPS, somnolence, weight, BMI, lipids, glucose,	Although improvements in PANSS total score at day 56 of the acute phase were numerically greater

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
centers) **Condition category:** Schizophrenia and related **Funding:** Industry **Risk of bias:** Low (subjective), Low (objective)	**Setting:** in and outpatient (mostly outpatient) **Diagnostic criteria:** DSM-IV-TR, K-SADS-PL **Inclusion criteria:** (1) 12-17 yrs, (2) schizophrenia, (3) PANSS total ≥80, CGI-S ≥4, and ≥4 on 2+ items on PANSS positive subscale **Exclusion criteria:** (1) treatment with clozapine, (2) comorbid Axis I condition responsible for current symptoms, (3) uncontrolled or unstable clinically significant general medical condition (eg, renal, endocrine, hepatic, respiratory, cardiovascular, hematologic, immunologic, or cerebrovascular disease, or malignancy) or an abnormal laboratory, vital sign, physical examination, or ECG findings), (4) uncontrolled diabetes or significant abnormal	**Age, mean±SD (range):** 15.4±1.5 **Males %: 63** **Caucasian %: 52** **Treatment naïve (n):** 33 **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 2** **N:** 98 **Age, mean±SD (range):** 15.2±1.5 **Males %:** 63 **Caucasian %: 55** **Treatment naïve (n):** 28 **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 3** **N:** 102 **Age, mean±SD (range):** 15.4±1.4 **Males %:** 61 **Caucasian %:** 56 **Treatment naïve (n):** 36 **Inpatients (n):** NR **First episode psychosis (n):** NR	equivalent; or diazepam £ 40 mg/day in countries with no approved short-acting benzodiazepines) for relief of transient symptoms of agitation, anxiety, insomnia, restlessness, or akathisia, and anticholinergics or short-acting benzodiazepines to treat EPS symptoms **Prohibited drugs:** antipsychotics; depot neuroleptics; antidepressants; benzodiazepines; mood stabilizers; stimulants and other ADHD medications; miscellaneous psychotropics; and herbal drugs/dietary supplements for depression, anxiety, and insomnia **GROUP 1** **Drug name:** Asenapine **Dosing variability:** fixed **Target dose (mg/day):** 5mg bid (2.5mg bid days 1-4; 5mg bid onwards) **Daily dose (mg/day), mean±SD (range):** **Concurrent treatments:** anti-EPS (12) **GROUP 2** **Drug name:** Asenapine **Dosing variability:** fixed **Target dose (mg/day):** 2.5mg bid **Daily dose (mg/day), mean±SD (range):** **Concurrent treatments:** anti-EPS (2) **GROUP 3** **Drug name:** Placebo	insulin, prolactin, metabolic syndrome, mortality, suicide, any AE, serious AEs,	for both asenapine 2.5 and 5mg b.i.d. than for placebo and were maintained in the OLE, the primary end-point did not achieve statistical significance in the acute phase.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	blood glucose, (5) suicide ideation over past 2 mo or behavior over past 6 mo, (6) beginning psychotherapy after trial initiation, (7) MR or SUD		**Dosing variability:** fixed **Target dose (mg/day):** NA **Daily dose (mg/day), mean±SD (range):** NA **Concurrent treatments:** anti-EPS (3)		
Findling et al., 2014b [27] **Country:** USA **Condition category:** ASD **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** Mar 2011 to Jun 2012 **Study design:** RCT (parallel) **Setting:** NR **Diagnostic criteria:** DSM-IV-TR, ADI-R **Inclusion criteria:** (1) Male of female, (2) 6-17 yr, (3) meets DSM-IV-TR criteria for autistic disorder, confirmed by ADI-R and also had serious behavioural problems (ie, tantrums, aggression, self-injurious behaviour, or a combination of these), (4) ABC-I score ≥18, CGI-S score ≥4 at screening and baseline **Exclusion criteria:** (1) Treatment resistant to antipsychotic medication (lack of therapeutic response to 2 different antipsychotics with	**Enrolled:** 85 **Analyzed:** 82 **Completed:** 41 **GROUP 1** **N:** 41 **Age, mean±SD (range):** 10.1±2.8 yr **Males %:** 73.2 **Caucasian %:** 75.6 **Diagnostic breakdown (n):** ASD (all) **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 44 **Age, mean±SD (range):** 10.8±2.8 yr **Males %:** 86.4 **Caucasian %:** 63.6 **Diagnostic breakdown (n):** ASD (all) **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR	**Treatment duration:** 16 wk **Run–in phase:** No **Run–in phase duration:** NA **Permitted drugs:** Diphenhydramine for sleep or serious behaviour problems, nonbenzodiazepine sleep aids (eg, zolpidem, zaleplon, zopiclone, eszopiclone) for insomnia, and melatonin for insomnia (not permitted to start or make changes to their sleep aid treatment durng phase 2) **Prohibited drugs:** Antipsychotics other than aripiprazole, antidepressants, benzodiazepines, stimulants, α-agonists, mood stabilizers, and atomoxetine **GROUP 1** **Drug name:** Aripiprazole **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 9.0±4.5 [initial of phase 2], 9.7±4.9 [end dose at wk 16] **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD**	**Benefits:** ABC-I, CGI-I, CGI-S, PedsQL, CGSQ, relapse, medication adherence **Harms:** Constipation, EPS (AIMS, BAS, SAS), akathisia, mortality, lipid profile, glucose, prolactin, sexual maturation	The safety and efficacy of aripiprazole and risperidone were comparable. The choice between these two medications should be on the basis of clinical equipoise considering the patient's preference and clinical profile.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	treatment of ≥3 wks each) or previously treated with an adequate dose of aripiprazole for ≥3 wks without a clinically meaningful response, (2) lifetime dx of bipolar disorder, psychosis, or shizophrenia or a current dx of major depressive disorder, pervasive developmental disorder-NOS, Asperger syndrome, Rett syndrome, childhood disintegrativedisorder, or fragile X syndrome, (3) hisory of neoroleptic malignant syndrome, history of seizures within the past year or of severe head trauma or stroke, a history or current unstable medical conditions, a history of low white blood cell count, or abnormal laboratory test results that were medically significant		**(range):** 9.5±4.2 [initial of phase 2], 10.0±4.2 [end dose at wk 16] **Concurrent treatments:** NR		
Findling et al., 2014a [26] **Country:** USA **Condition category:** Bipolar	**Recruitment dates:** Jan 2009 to Nov 2010 **Study design:** RCT (parallel) **Setting:** Outpatient	**Enrolled:** 193 **Analyzed:** 192 **Completed:** 144 **GROUP 1** **N:** 92 **Age, mean±SD (range):**	**Treatment duration:** 8 wk **Run-in phase:** Yes **Run-in phase duration:** 7-28 d **Permitted drugs:** Psychostimulants (centrally acting sympathomimetics, including amphetamine,	**Benefits:** CDRS-R, CGI-BP-S, CGI-BP-C, response, remission, suicidal ideation, aggression, medication adherence, health	QuetiapineXR(150 to 300 mg/day) did not demonstrate efficacy relative to placebo in this large, 8 week, randomized study of

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
I,II (depressed) **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Diagnostic criteria:** DSM-IV-TR, K-SADS-PL **Inclusion criteria:** (1) Boys and girls, (2) 10–17 yr, (3) dx of bipolar I or bipolar II disorder, current or most recent episode depressed; duration ≥4 wk (DSM-IV-TR, confirmed by K-SADS-PL), (4) CDRS-R total score ≥45 (5) YMRS score ≤16 at screening and baseline, (6) Patients with rapid cycling, defined as ≥4 episodes/yr, and a secondary diagnosis of comorbid ADHD, were permitted **Exclusion criteria:** (1) current DSM-IV-TR Axis I disorder other than bipolar I or bipolar II depression or ADHD, (2) YMRS total score >16 at screening or baseline, (3) criteria for bipolar disorder, most recent episode mania/ hypomania/ mixed, as determined by the K-SADS-PL, (4) history of nonresponse to adequate treatment with more than two antidepressants during	13.9±2.2 yr **Males %:** 48.9 **Caucasian %:** 70.7 **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** ADHD (38) **GROUP 2** **N:** 100 **Age, mean±SD (range):** 14.0±2.1 yr **Males %:** 52.0 **Caucasian %:** 60.0 **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** ADHD (46)	dexamphetamine, methylphenidate) in patients with ADHD if prescribed dose stable ≥30 d prior to baseline. No dose adjustment allowed during study. Nonpsychoactive medications considered necessary for patient's well being **Prohibited drugs:** Adjunctive medications for EPS **GROUP 1** **Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** 300 **Daily dose (mg/day), mean±SD (range):** mean modal dose, 204.9mg/day **Concurrent treatments: Total** psychostimulants (20), other (35) **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** psychostimulants (27), other (37)	care system utilization, exacerbation of bipolar I and depressive symptoms, mania (YMRS) **Harms:** somnolence, fatigue, nausea, agitation, EPS (AIMS, BAS, SAS), ECG, transaminase, fasting glucose, dyslipidemia, TSH, throxine, prolactin, weight gain, blood pressure, pulse	youth with bipolar I or II depression. These observations contrast with the efficacy of quetiapine XR demonstrated in adults with bipolar de-pression or MDD. Consistent with studies in adults, quetiapine XR at the dose range investigated was generally safe and well tolerated in these pediatric patients.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	the current episode or of treatment noncompliance, (5) use of valproate within 3 days, an antipsychotic, other mood stabilizer, antidepressant, an-xiolytic, hypnotic, or other psychoactive drug within 7 days, or fluoxetine within 28 days before baseline, (6) a requirement for psychotherapy during the study period, unless initiated at least 3 mo before, (7) being a current serious suicidal or homicidal risk, CDRS-R intem 13 score ≥3 at enrollment or randomization, (8) clinically significant deviations from normal reference ranges of clinical laboratory parameters				
Findling, 2013a [24] **Country:** Canada, Columbia, Costa Rica, Germany, India, Malaysia, Mexico, Peru, Russia, Singapore, Sweden, Ukraine, USA **Condition category:**	**Recruitment dates:** Apr 2006 to Mar 2009 (terminated prematurely) **Study design:** RCT (parallel) **Setting:** In- and outpatient **Diagnostic criteria:** DSM-IV, KID-SCID	**Enrolled:** 284 **Analyzed:** 283 **Completed:** NR **GROUP 1** **N:** 193 **Age, mean±SD (range):** 15.3 **Males %:** 56 **Caucasian %:** 60 **Diagnostic breakdown (n):** paranoid type (127) **Treatment naïve (n):** NR	**Treatment duration:** 6 wk **Run-in phase:** Yes **Run-in phase duration:** 14 days **Permitted drugs:** lorazepam or diazepam, diphenhydramine, zolpidem, benzotropine, anticholinergics, propranolol **Prohibited drugs:** antipsychotic, mood stabilizers, stimulants, antidepressants, anti-emetics, several antihypertensives	**Benefits:** BPRS-A, PANSS, CGI-S, CGI-I, CGAS, health related quality of life (Child Health Questionnaire), suicide, depression **Harms:** Serious AE, SARS, BARS, AIMS, akathisia, behavioral issues, dermatologic AE, ECG changes,	Oral ziprasidone failed to demonstrate superiority over placebo in adolescents with schizophrenia.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Schizophrenia and related **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Inclusion criteria:** (1) 13–17 yr, (2) schizophrenia (DSM-IV, confirmed by KID-SCID), (3) current symptoms present for ≥7 days prior to screening, (4) first episode psychosis allowed, (5) BPRS Anchored score ≥35 and a score ≥4 on ≥1 of the following items: unusual thought content, hallucinations, suspiciousness, or conceptual disorganization at screening and baseline visits, (6) BMI Z-score 1.65–2.00, inclusive **Exclusion criteria:** substance-induced psychotic disorder, a DSM-IV–defined psychoactive substance or alcohol abuse/ dependence in the preceding month, a rating of 7 on the single suicidal ideation item on the Child Depression Rating Scale-Revised (CDRS-R), significant MR, or ASD, or if they were judged by investigator to be at imminent risk of suicide or homicide. Other general criteria	**Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 2** **N:** 90 **Age, mean±SD (range):** 15.4 **Males %:** 69 **Caucasian %:** 67 **Diagnostic breakdown (n):** paranoid type (57) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR	**GROUP 1** **Drug name:** Ziprasidone **Dosing variability:** variable **Target dose (mg/day):** 40–80 (<45 kg), 120–160 (≥45 kg) **Daily dose (mg/day), mean±SD (range):** 67.8 (<45kg), 129.3 (≥45kg) **Concurrent treatments:** 51% **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** 60–80 (<45 kg), 120–160 (≥45 kg) **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** 39%	QTcF, fatigue, EPS, liver function, mortality, SAE, somnolence, total AE, WAE, weight change, blood pressure, pulse rate, lipids	

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	for exclusion included serious/ unstable medical conditions, history of significant cardiovascular disease, cardiac arrhythmias, conduction abnormalities, QT prolongation, clinically significant ECG abnormalities, and Fridericia's corrected QT (QTcF) interval ‡460ms at screening or baseline.				
Findling et al., 2013b [25] **Country:** USA **Condition category:** Bipolar I (manic, mixed) **Funding:** Industry, non-industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** Jan 2006 to Jul 2007 **Study design:** RCT (parallel) **Setting:** NR **Diagnostic criteria:** DSM-IV, K-SADS **Inclusion criteria:** (1) 10–17 yr, (2) primary dx of bipolar I disorder (DSM-IV, confirmed by K-SADS), (3) current symptoms present for ≥7 day prior to screening, (4) YMRS score >17 at screening and baseline visits, (5) BMI Z-score 1.65–2.00, inclusive **Exclusion criteria:** (1) current or prior	**Enrolled:** 238 **Analyzed:** 229 **Completed:** 148 **GROUP 1** **N:** 149 **Age, mean±SD (range):** 13.2±2.4 yr (males), 14.1±2.0 yr (females) **Males %:** 56.4 **Caucasian %:** 81.2 **Diagnostic breakdown (n):** Single manic (14), manic (45), mixed (90) **Treatment naïve (n):** 149 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (66) **GROUP 2** **N:** 88 **Age, mean±SD (range):** 13.5±2.0 yr (males), 14.0±1.9 yr (females)	**Treatment duration:** 4 wk **Run-in phase:** Yes **Run-in phase duration:** 1–10 day **Permitted drugs:** Lorazepam or a comparable benzodiazepine as required ≤2mg/day. Not to be administered ≤6 hours prior to clinical assessments. **Prohibited drugs:** Other antipsychotics, lithium and anticonvulsants, stimulants, antidepressants, antiemetics (dopamine antagonists such as prochlorperazine and metoclopramide), treatment with clozapine ≤12 weeks, treatment with a depot antipsychotic ≤4 weeks, treatment with a monoamine oxidase inhibitor ≤2 weeks, or treatment with an investigational agent ≤4 weeks of baseline. **GROUP 1** **Drug name:** Ziprasidone	**Benefits:** YMRS, CGI-S, CGI-I, CGAS, CDRS-R, suicidal ideation, aggression **Harms:** dystonia, akathisia, dyskinesia, EPS (AIMS, BAS, SARS), somnolence, weight change, nausea, prolonged QTc interval, increased hepatic enzymes, extrapyramidal disorder, self-injurious behavior, prolactin, lipid profile, fatigue	Ziprasidone at doses of 40–160 mg/day is an effective and generally well-tolerated treatment for children and adolescents 10–17 years of age with a manic or mixed episode associated with bipolar I disorder.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	treatment with ziprasidone, (2) known allergy to ziprasidone, (3) serious suicidal risk, (4) a Fridericia-corrected QT interval (QTcF) ≥460 ms, (5) DSM-IV substance abuse/dependence (except nicotine or caffeine) in the preceding month, and (5) numerous other standard medical and psychiatric exclusion criteria	**Males %:** 53.4 **Caucasian %:** 81.8 **Diagnostic breakdown (n):** Single manic (8), manic (23), mixed (57) **Treatment naïve (n):** 88 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (36)	**Dosing variability:** variable **Target dose (mg/day):** 60–80 (<45 kg), 120–160 (≥45 kg) **Daily dose (mg/day), mean±SD (range):** 69.2(<45 kg), 118.8 (≥45 kg) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** 60–80 (<45 kg), 120–160 (>45 kg) **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR		
Findling et al., 2012b [23] **Country:** USA **Condition category:** Bipolar I,II, NOS, cyclothymia **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** May 2004 to Nov 2008 **Study design:** RCT (parallel) **Setting:** Outpatient **Diagnostic criteria:** DSM-IV, K-SADS-PL **Inclusion criteria:** (1) 4-9 yr, (2) met DSM-IV criteria for bipolar I, II, NOS or cyclothymia, (3) screened by highly trained raters completing K-SADS-PL, (4) patients must have adhered to study-related procedures during phase 1, (5) tolerated a minimum daily aripiprazole dose of 0.05 mg/kg/day for	**Enrolled:** 60 **Analyzed:** 60 **Completed:** 6 **GROUP 1** **N:** 30 **Age, mean±SD (range):** 7.1±1.5 yr **Males %:** 63 **Caucasian %:** NR **Diagnostic breakdown (n):** bipolar disorder NOS (17), bipolar I disorder (10), cyclothymia (3) **Treatment naïve (n):** 0 **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** DBD (6), ADHD (27), any anxiety disorder (0) **GROUP 2** **N:** 30 **Age, mean±SD (range):**	**Treatment duration:** 72 wk (after 16 wk of open label study: phase I) **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** Continued coadministration of stable dose of psychostimulants from phase 1 **Prohibited drugs:** Other psychotropic medications **GROUP 1** **Drug name:** Aripiprazole **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 0.23±0.07 [at randomization], 0.26±0.11 [end of study] **Concurrent treatments:** Stimulants (12) **GROUP 2** **Drug name:** Placebo	**Benefits:** YMRS, CDRS-R, CGAS, CGI-S, time to discontinuation of medication **Harms:** weight, EPS (AIMS, BAS, SAS), lipid values, prolactin, fasting glucose, blood pressure, pulse, mortality	Even though aripiprazole maintenance was statistically superior to placebo maintenance, alone it was not sufficient to keep most youth stable for extended periods of time.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	at least 6 wk, (6) met a priori response criteria **Exclusion criteria:** (1) evidence of pervasive developmental disorder, Rett's syndrome, mental retardation, (2) a general medical or neurologic condition for which treatment with aripiprazole would be contraindicated	6.7±1.7 yr **Males %:** 77 **Caucasian %:** NR **Diagnostic breakdown (n):** bipolar disorder NOS (16), bipolar I disorder (11), cyclothymia (3) **Treatment naïve (n):** 0 **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** DBD (5), ADHD (27), any anxiety disorder (2)	**Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 0.22±0.07 [at randomization], 0.22±0.07 [end of study] **Concurrent treatments:** Stimulants (13)		
Findling et al., 2012a [22] **Country:** Asia, Central and Eastern Europe, South Africa, United States **Condition category:** Schizophrenia and related **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** Oct 2004 to June 2007 **Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV, K-SADS-PL **Inclusion criteria:** (1) inpatients and outpatients, (2) 13–17 yr, (3) schizophrenia (DSM-IV, confirmed by K-SADS-PL), (4) PANSS total score ≥60 and a score ≥4 on delusions, conceptual disorganization, or hallucinations **Exclusion criteria:** DSM-IV Axis I diagnosis of BD,	**Enrolled:** 222 **Analyzed:** 220 **Completed:** 220 **GROUP 1** **N:** 73 **Age, mean±SD (range):** 15.5±1.3 (13–17) **Males %:** 58.9 **Caucasian %:** 61.6 **Diagnostic breakdown (n):** disorganized (6), paranoid (53), residual (0), undifferentiated (14) **Treatment naïve (n):** NR **Inpatients (n):** 31 **First episode psychosis (n):** NR **GROUP 2** **N:** 74 **Age, mean±SD (range):** 15.5±1.3 (13–17) **Males %:** 59.5 **Caucasian %:** 59.5 **Diagnostic breakdown (n):** disorganized (5),	**Treatment duration:** 6 wk **Run-in phase:** Yes **Run-in phase duration:** 1 day–4 wk **Permitted drugs:** antidepressants, lorazepam **Prohibited drugs:** antipsychotics, psychostimulants, CYP3A4 inhibitors/inducres, monoamine oxidase inhibitors, atomoxetine, prophylactic benztropine **GROUP 1** **Drug name:** Quetiapine (low) **Dosing variability:** fixed **Target dose (mg/day):** 400 **Daily dose (mg/day), mean±SD (range):** 400 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Quetiapine (high) **Dosing variability:** fixed **Target dose (mg/day):** 800 **Daily dose (mg/day), mean±SD	**Benefits:** BSPSd, CGAS, CGI-I, CGI-S, PANSS, Caregiver Strain Questionnaire, response, agitation, aggression, medication adherence **Harms:** Withdrawals from AEs, serious AEs, SAS, BARS, AIMS-7, behavioral issues, ECG changes, EPS, fatigue, lipid profile, glucose concentration, mortality, prolactin, pulse, SAE, sedation, somnolence, tachycardia, thyroid, liver and renal function, total AE, WAE, weight change	Quetiapine at a dose of 400 mg/day and 800 mg/day provided significant improvements in symptoms associated with schizophrenia in adolescent patients, including the primary efficacy measure of PANSS total score change. Quetiapine was generally well tolerated with a profile broadly similar to that reported previously in adult and adolescent populations.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	schizophreniform disorder, schizoaffective disorder, psychotic disorder NOS, or acute PTSD, psychosis judged to be a direct consequence of a medical condition or its treatment, history of suicide attempts or homicidal risk or behavior within the past 3 months, DSM-IV-defined SUD, laboratory test results outside the normal reference range, hospital admission for diabetes or diabetes-related illness in the past 3 months, renal, cardiovascular, hepatic, hematologic, endocrinologic, ophthalmologic, or other medical conditions that were unstable or may have affected or been affected by the study medication, pregnancy and lactation.	paranoid (50), residual (1), undifferentiated (18) **Treatment naïve (n):** NR **Inpatients (n):** 28 **First episode psychosis (n):** NR **GROUP 3** **N:** 73 **Age, mean±SD (range):** 15.3±1.4 (13–17) **Males %:** 57.5 **Caucasian %:** 63 **Diagnostic breakdown (n):** disorganized (5), paranoid (52), residual (0), undifferentiated (16) **Treatment naïve (n):** NR **Inpatients (n):** 36 **First episode psychosis (n):** NR	**(range):** 800 **Concurrent treatments:** NR **GROUP 3** **Drug name:** Placebo **Dosing variability: fixed** **Target dose (mg/day):** NA **Daily dose (mg/day), mean±SD (range):** NA **Concurrent treatments:** NR		
Findling et al., 2009 [21] **Country:** USA **Condition category:** Bipolar (manic, mixed)	**Recruitment dates:** Mar 2005 to Feb 2007 **Study design:** RCT (parallel) **Setting:** Inpatient and outpatient	**Enrolled:** 296 **Analyzed:** 294 **Completed:** 237 **GROUP 1** **N:** 98 **Age, mean±SD (range):** 13.7±2.2 **Males %:** 53.1	**Treatment duration:** 4 wk **Run-in phase:** Yes **Run-in phase duration:** 3 day **Permitted drugs:** anticholinergics, benzodiazepines **Prohibited drugs:** Mood stabilizers, other psychotropics	**Benefits:** CDRS, CGAS, CGI-BP, YMRS, health related quality of life (P-QLES-Q), response, suicide **Harms:** Akathisia, BMI, dyskinesia,	Aripiprazole in daily doses of 10 mg or 30 mg was effective and generally well-tolerated for acute treatment of pediatric subjects with bipolar I mania or mixed episodes.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Funding: Industry **Risk of bias:** Medium (subjective), Medium (objective)	**Diagnostic criteria:** DSM-IV, K-SADS-PL **Inclusion criteria:** (1) 10–17 yr, (2) bipolar I disorder with current manic or mixed episodes, with or without psychotic features (DSM-IV), (3) YMRS score ≥20 **Exclusion criteria:** (1) bipolar II disorder, bipolar disorder NOS, PDD, schizophrenia, schizoaffective disorder, psychosis due to other medical condition or concomitant medication, (2) MR, (3) DSM-IV substance or alcohol use disorder, (4) positive drug screen for cocaine or other substances of abuse during screening, (5) sexual activity without contraceptive use, pregnancy, lactation, (6) other medical reason determined by investigator, (7) noncompliance with medication washout, (8) inability to swallow tablets whole, (9) history of antipsychotic treatment resistance or NMS, (10) suicide	**Caucasian %:** 66.3 **Diagnostic breakdown (n):** manic (41), mixed (43), unknown (14) **Treatment naïve (n):** 41 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (48), DBD (28) **GROUP 2** **N:** 99 **Age, mean±SD (range):** 13.3±2.3 **Males %:** 51.5 **Caucasian %:** 68.7 **Diagnostic breakdown (n):** manic (40), mixed (39), unknown (20) **Treatment naïve (n):** 49 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (50), DBD (34) **GROUP 3** **N:** 99 **Age, mean±SD (range):** 13.3±2.1 **Males %:** 56.6 **Caucasian %:** 60.6 **Diagnostic breakdown (n):** manic (38), mixed (43), unknown (18) **Treatment naïve (n):** 36 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (55), DBD (31)	**GROUP 1** **Drug name:** Aripiprazole (low) **Dosing variability:** variable **Target dose (mg/day):** 10 **Daily dose (mg/day), mean±SD (range):** (2–10) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Aripiprazole (high) **Dosing variability:** variable **Target dose (mg/day):** 30 **Daily dose (mg/day), mean±SD (range):** (2–30) **Concurrent treatments:** NR **GROUP 3** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	dystonia, ECG changes, EPS (AIMS, BAS, SAS), fatigue, glucose, lipid profile, mortality, parkinsonism, prolactin, SAE, somnolence, total AE, WAE, weight change	

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	attempt in the past 6 mo, score >3 on the Suicidal Ideation item of the CDRS-R, or determined by the investigator to be at risk of suicide, (11) clinically important laboratory test results, vital signs, or ECG, and unstable medical conditions, diabetes melitus, epilepsy, (12) prior participation in an aripiprazole study, allergy or hypersensitivity to aripiprazole, or participation in an investigational drug trial in the past month				
Findling et al., 2008a [20] **Country:** Asia, Caribbean, Europe, South Africa, South America, USA **Condition category:** Schizophrenia and related **Funding:** Industry **Risk of bias:** Medium (subjective), Medium (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV, K-SADS-PL **Inclusion criteria:** (1) 13–17 yr, (2) primary dx of schizophrenia (DSM-IV Axis I, confirmation with K-SADS-PL), (3) baseline PANSS ≥ 70 **Exclusion criteria:** (1)	**Enrolled:** 302 **Analyzed:** 294 **Completed:** 258 **GROUP 1** **N:** 100 **Age, mean±SD (range):** 15.6±1.3 **Males %:** 45 **Caucasian %:** 54 **Diagnostic breakdown (n):** For all: schizophrenia (1), BP (12), Tourette syndrome (5), ADHD/CD (1), OCD (1), PDD (1) **Treatment naïve (n):** 25 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR	**Treatment duration:** 6 wk **Run-in phase:** Yes **Run-in phase duration:** ≥3 day **Permitted drugs:** anticholinergics, benzodiazepines **Prohibited drugs:** antidepressants, atomoxetine, mood stabilizers, other psychotropics, stimulants **GROUP 1** **Drug name:** Aripiprazole (low) **Dosing variability:** variable **Target dose (mg/day):** 10 **Daily dose (mg/day), mean±SD (range):** 9.8 (2–10) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Aripiprazole (high)	**Benefits:** CGAS, CGI-I, CGI-S, PANSS Health related quality of life (P-QLES-Q), response, suicide **Harms:** Akathisia, behavioral issues, BMI, dyskinesia, dystonia, ECG changes, EPS, EPS (SAS), glucose, lipid profile, mortality, prolactin, parkinsonism, SAE, somnolence, WAE, weight change	Aripiprazole (10 or 30 mg/d) was well tolerated and was more effective than placebo in improving symptoms of schizophrenia.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	current psychiatric comorbidity requiring pharmacology, (2) evidence of suicide risk, (3) history, or current dx of schizoaffective disorder, MR, major depressive episodes, NMS, any neurologic disorder other than Tourette syndrome, severe head trauma, unstable medical condition, (4) resistant to antipsychotics according to trials of two different antipsychotics of adequate dose and duration, (5) pregnancy, breast-feeding, sexually active patients who refused abstinence or birth control, (6) positive screens for illegal drugs within 3 mo of baseline or during study, (7) hospitalized for acute schizophrenia within 4 wk of baseline	**GROUP 2** **N:** 102 **Age, mean±SD (range):** 15.4±1.4 **Males %:** 63.7 **Caucasian %:** 60.8 **Diagnostic breakdown (n):** See group 1 **Treatment naïve (n):** 27 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 3** **N:** 100 **Age, mean±SD (range):** 15.4±1.4 **Males %:** 61 **Caucasian %:** 64 **Diagnostic breakdown (n):** See group 1 **Treatment naïve (n):** 27 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR	**Dosing variability:** variable **Target dose (mg/day):** 30 **Daily dose (mg/day), mean±SD (range):** 28.9 (2–30) **Concurrent treatments:** NR **GROUP 3** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR		
Findling et al., 2008b [104] **Country:** USA **Condition category:** Mixed conditions **Funding:** Industry	**Recruitment dates:** NR **Study design:** OLE **Setting:** NR **Diagnostic criteria:** **Inclusion criteria:** (1)	**Enrolled:** 24 **Analyzed:** 21 (safety); 20 (efficacy) **Completed:** 17 **All** **N:** 21 **Age, mean±SD (range):** 12.2±2.1 **Males %:** 66.7	**Treatment duration:** 26 d **Run-in phase:** NR **Run-in phase duration:** NR **Concurrent treatments:** Analgesics (paracetamol; Vicks formula 44M) (5); anesthetics (lidocaine) (4); antiasthmatics (budesonide; salbutamol; other) (2); antiparkinsonism drugs	**Benefits:** CGI-I/S **Harms:** AEs, physical examination, vital signs, ECGs, clinical laboratory parameters, and EPS (SAS, AIMS, BARS)	Aripiprazole at doses of 20, 25, and 30 mg/d seemed generally safe and well tolerated in children and adolescents with psychiatric disorders. All 3 planned aripiprazole

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Newcastle-Ottawa Scale: 5/8 stars	13-17 yr; (2) dx of schizophrenia or bipolar **Exclusion criteria:** (1) sexually active pt not practicing double-barrier birth control; (2) pregnancy/lactation; (3) current/hx of drug or alcohol abuse; (4) mental retardation; (5) neurologic disorders (except PDD, ADHD, or TS); (6) use of antipsychotic or psychotropic medication, CYP2D6 and CYP3A4 inhibitors, or CYP3A4 inducers <14 d; (7) participation in another clinical study <1 mo (or 6 mo if the study involved psychotropic medication); (8) major surgery or blood transfusion/donation <30 d; (9) abnormal physical, ECG, or clinical laboratory examinations; (10) significant risk of suicide or homicide	**Caucasian %:** 76.1 **Diagnostic breakdown (n):** schizophrenia (1); bipolar disorder (12); TS (5); ADHD and CD (1); OCD (1); PDD (1) **Treatment naïve (n):** **Inpatients (n):** **First episode psychosis (n):** **Comorbidities:** GROUP **1** **N:** 8 **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 7 **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 3** **N:** 6	(benztropine; benztropine mesylate) (2); anti-inflammatories or antirheumatics (naproxen sodium; ibuprofen) (2); antipruritics including antihistamines (diphenhydramine hydrochloride) (1); antacids (dihydroxyaluminum sodium carbonate) (1); antibacterials (minocycline) (1); sex hormones (progestogens and estrogens) (1); antidiabetics (insulin lispro; insulin and analog) (1); nasal preparations (Dimetapp) (1) **GROUP 1** **Drug name:** Aripiprazole **Dosing variability:** 2 mg/d (starting dose), then increased to target dose every 2 d for 8 d **Target dose (mg/day):** 20 mg/d **Daily dose (mg/day), mean±SD (range):** NR **GROUP 2** **Drug name:** Aripiprazole **Dosing variability:** 2 mg/d (starting dose), then increased to target dose every 2 d for 10 d **Target dose (mg/day):** 25 mg/d **Daily dose (mg/day), mean±SD (range):** NR **GROUP 3** **Drug name:** Aripiprazole **Dosing variability:** 2 mg/d (starting dose), then increased to target dose every 2 d for 12 d **Target dose (mg/day):** 30 mg/d **Daily dose (mg/day), mean±SD (range):** NR		dose levels were judged to be tolerated.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Age, mean±SD (range): NR **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR			
Findling et al., 2000 [19] **Country:** USA **Condition category:** ADHD **Funding:** Industry, Foundation **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV, K-SADS, clinical interview **Inclusion criteria:** (1) outpatients with primary dx of CD, (2) 5–15 yr, (3) at least moderate degree of overall symptom severity (CGI), (4) Aggression subscale T-score ≥2 SD above the mean for age- and gender-matched peers (CBCL) **Exclusion criteria:** (1) moderate/severe ADHD, (2) significant psychiatric comorbidity (including mood	**Enrolled:** 20 **Analyzed:** 20 **Completed:** 9 **GROUP 1** **N:** 10 **Age, mean±SD (range):** 10.7±3.4 yr **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown:** CD with aggression (10) **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 10 **Age, mean±SD (range):** 8.2±1.9 yr **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown:** CD with aggression (10) **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** NR	**Treatment duration:** 10 wk **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** benztropine **Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 0±0.004 (0.8–1.5) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** (0.3–3) **Concurrent treatments:** NR	**Benefits:** CBCL, CGI-I, CGI-S, Conner PRS, RAAPP Medication adherence **Harms:** Dermatologic AE, EPS, liver function, sedation, total AE, WAE, AIMS, SAS	Low doses of risperidone may be effective in the treatment of youths with CD and are not associated with extrapyramidal symptoms.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	disorder), (3) treatment with a psychotropic medication within 1 wk of initiating double-blind therapy, (4) positive toxicology screen, (5) suicide attempt within the past mo, (6) organic mental syndromes, (7) pregnant or nursing females and females of childbearing potential who were not using an acceptable method of birth control, (8) a standard score equivalent to <70 on the Peabody Picture Vocabulary Test-Revised				
Fleischhaker et al., 2006 [105] **Country:** Germany **Condition category:** Mixed conditions **Funding:** NR **Newcastle-Ottawa Scale:** 3/8 stars	**Recruitment dates:** NR **Study design:** Prospective cohort **Setting:** Inpatient **Diagnostic criteria:** ICD-10 **Inclusion criteria:** NR **Exclusion criteria:** NR	**Enrolled:** 51 **Analyzed:** 51 **Completed:** 51 **GROUP 1** **N:** 16 **Age, mean±SD (range):** 17.2±1.8 (14.4–21.3) **Males %:** 68.9 **Caucasian %:** NR **Treatment naïve (n):** NR **Diagnostic breakdown (n):** Schizophrenia (31), PDD (5), AN (1), Cannabis-related disorders (4), AD (3), DBD (3), OCD (2), TD (1) for all groups **Inpatients (n):** NR **First episode psychosis (n):** NR	**Treatment duration:** 7.4 wk (mean) **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Clozapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 321.9±156.5 (125–600) **Concurrent treatments:** all groups: amisulpride, biperiden, chlorprotixene, fluboxamine, fluoxetine, haloperidol, imipramine, lactulose, levomepromazine, lorazepam, metixene, metoclopramid, metoprolol,	**Benefits:** NR **Harms:** Akathisia, behavioral issues, bradycardia, blood cells, blood pressure, BMI, constipation, dystonia, dermatologic AE, ECG changes, liver function tachycardia, tardive dyskinesia, weight change	Olanzapine caused significant weight gain in children and adolescents, potentially influencing medication compliance and health risk. Clozapine and risperidone were associated with less marked changes in weight, but gains were still more pronounced than those seen in adults.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Comorbidities (n): NR **GROUP 2** **N:** 16 **Age, mean±SD (range):** 15.8±1.4 (12.8–17.8) **Males %:** 56.3 **Caucasian %:** NR **Treatment naïve (n):** NR **Diagnostic breakdown (n):** See group 1 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** NR **GROUP 3** **N:** 19 **Age, mean±SD (range):** 15.6±2.6 (9.7–19) **Males %:** 68.4 **Caucasian %:** NR **Treatment naïve (n):** NR **Diagnostic breakdown (n):** See group 1 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** NR	paroxetine, perazine, pimozide, pipamperone, pirenzepine, promethazine **GROUP 2** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 16.6±7.1 (7.5–30) **Concurrent treatments:** see group 1 **GROUP 3** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 3.9±1.7 (1–6) **Concurrent treatments:** see group 1		
Fraguas et al., 2008 [106] **Country:** Spain **Condition category:** Mixed conditions **Funding:** Government, Foundation, Other	**Recruitment dates:** Mar 2005 to Oct 2006 **Study design:** Prospective cohort **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV	**Enrolled:** 92 **Analyzed:** 66 **Completed:** 66 **GROUP 1** **N:** 25 **Age, mean±SD (range):** 15.9±1.5 (12–17) **Males %:** 65 **Caucasian %:** 90 **Diagnostic breakdown (n):** bipolar (2),	**Treatment duration:** 6 mo **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** anticholinergics, antidepressants, benzodiazepines **Prohibited drugs:** antipsychotics **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** variable	**Benefits:** NR **Harms:** Blood pressure, BMI, glucose, lipid profile, thyroid function, weight change	Metabolic and hormonal adverse events should be carefully monitored when prescribing SGAs.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
NR **Newcastle-Ottawa Scale:** 6/8 stars	**Inclusion criteria:** (1) new prescription of olanzapine, risperidone of quetiapine within 30 days, (2) no history of prior lifetime antipsychotic treatment **Exclusion criteria:** (1) receiving >1 antipsychotic or needed another antipychotic during followup	depression (1), eating disorders (3), PDD (1), psychosis NOS (5), schizophrenia (3), schizophreniform (5) **Treatment naïve (n):** 9 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** psychosis (14), SA (12) **GROUP 2** **N:** 29 **Age, mean±SD (range):** 16.3±1.3 (13–18) **Males %:** 58.3 **Caucasian %:** 95.8 **Diagnostic breakdown (n):** ADHD (0), bipolar (5), CD (1), depression (2), eating disorders (2), OCD (2), PDD (0), psychosis NOS (4), schizophrenia (4), schizophreniform (4) **Treatment naïve (n):** 8 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** psychosis (14), SA (18) **GROUP 3** **N:** 38 **Age, mean±SD (range):** 13.4±4 (4–17) **Males %:** 77.3 **Caucasian %:** 81.8 **Diagnostic breakdown (n):** ADHD (4), bipolar (1), CD (7), depression (1), eating disorders (1), OCD	**Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 9.8±5.6 **Concurrent treatments:** antidepressants (3), benzodiazepines (14), biperiden (4) **GROUP 2** **Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 390.8±321.2 **Concurrent treatments:** antidepressants (9), benzodiazepines (12), biperiden (4) **GROUP 3** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 3.5±3.1 **Concurrent treatments:** antidepressants (9), benzodiazepines (11), biperiden (6)		

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		(2), PDD (1), psychosis NOS (3), schizophrenia (2), schizophreniform (0) **Treatment naïve (n):** 8 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** psychosis (6), SA (13)			
Friedlander et al., 2001 [107] **Country:** Canada **Condition category:** Mixed conditions **Funding:** NR **Newcastle-Ottawa Scale:** 4/8 stars	**Recruitment dates:** NR **Study design:** Retrospective cohort **Setting:** NR **Diagnostic criteria:** DSM-IV, author consensus on chart review **Inclusion criteria:** (1) 13–24 yr, (2) developmental disabilities and complex psychiatric problems, (3) active files with the mental health sites in the Greater Vancouver area **Exclusion criteria:** NR	**Enrolled:** 44 **Analyzed:** 44 **Completed:** NR **GROUP 1** **N:** 14 **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** NR **Diagnostic breakdown (n):** Developmental disabilities (all), Schizophrenia/other psychotic (15), PDD (16), mood disorders (11), ADHD/DBD (6), Tic-related disorders (3), AD (2), Impulse control disorder (1) for all patients **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** Addison's disease (1), hypothyroidism (4), MR (borderline (1), mild (17), moderate (15), severe (9)), Neurodevelopmental syndrome (15), Seizure disorder (9)	**Treatment duration:** 6 wk **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** all groups: anticholinergics (5), anticonvulsants (12), anxiolytics (9), clonidine (1), mood stabilizers (21), non-SSRI antidepressants (8), SSRIs (9), stimulants (2), tetrabenazine (2) **GROUP 2** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** see group 1	**Benefits:** NR **Harms:** Akathisia, dyskinesia, dystonia, EPS, prolactin-related AE, sedation, total AE, WAE, weight change	Adolescents and young adults with developmental disabilities treated with SGAs for multiple conditions were particularly sensitive to neuroleptic induced movement disorders.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		GROUP 2 **N:** 40 **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** NR **Diagnostic breakdown (n):** see group 1 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** see group 1			
Germano et al., 2014 [108] **Country:** Italy **Condition category:** Mixed **Funding:** NR **Newcastle-Ottawa Scale:** 5/8 stars	**Recruitment dates:** Jan 2009-Dec 2012 **Study design:** Prospective **Setting:** NR **Diagnostic criteria:** NR **Inclusion criteria:** (1) child and adolescent pateints, (2) ≤17 yr **Exclusion criteria:** NR	**Enrolled:** 65 **Analyzed:** 60 **Completed:** 60 **GROUP 1** **N:** 29 **Age, mean±SD (range):** See below **Males %:** See below **Caucasian %:** NR **Diagnostic breakdown (n):** See below **Treatment naïve (n):** See below **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 31 **Age, mean±SD (range):** See below **Males %:** See below **Caucasian %:** NR **Diagnostic breakdown (n):** See below **Treatment naïve (n):** See	**Treatment duration:** 2 mo **Run-in phase:** Yes **Run-in phase duration:** 2 wk **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Aripiprazole **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 7.4±3.1 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Risperidone **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.5±1.0 **Concurrent treatments:** NR	**Benefits:** NR **Harms:** ECG parameters	Treatment with risperidone and aripiprazole in children and adolescents with psychiatric disorders is not associated with clinically relevant modifications of the QT interval on ECG. Aripiprazole use can be associated to a slight increase of QTd value only, along with risperidone use that can be associated to an increase of both QTc and QTd values. Therefore, monitoring of both QTc and QTd parameters during AP treatment in pediatric Population should be considered.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		below **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **Overall age, mean±SD (range):** 10.2±2.6 yr **Overall Males %:** 91.6 **Overall diagnostic breakdown (n):** PDD (22), ODD (12), ADHD (21), MR with psychotic disorder (11), Tourette syndrome and other tic disorders (9) **Overall treatment naïve (n):** 22			
Ghanizadeh et al., 2014a [30] **Country:** Iran **Condition category:** ASD **Funding:** Industry/ non-industry **Risk of bias:** Medium (subjective), Medium (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Outpatient **Diagnostic criteria:** DSM-IV-TR, ADI-R **Inclusion criteria:** (1) Meets DSM-IV-TR and ADI-R criteria,(2) has a clinicain rating of at least moderate severity of autistic symptoms (CGI severity score of C4) **Exclusion criteria:** (1) Children with a history of medically significant	**Enrolled:** 59 **Analyzed:** 59 **Completed:** 50 **GROUP 1** **N:** 29 **Age, mean±SD (range):** 9.6±3.3 yr **Males %:** 86.2 **Caucasian %:** NR **Diagnostic breakdown (n):** see below **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 30 **Age, mean±SD (range):** 9.5±4.6 yr **Males %:** 76.7	**Treatment duration:** 2 mo **Run–in phase:** NR **Run–in phase duration:** NR **Permitted drugs:** Any (with no marked change in dose allowed during the trial and during 2 wk before the trial onset) **Prohibited drugs:** Antipsychotics **GROUP 1** **Drug name:** Aripiprazole **Dosing variability:** variable **Target dose (mg/day):** 10 (<40 kg), 15 (>40kg) **Daily dose (mg/day), mean±SD (range):** 5.5 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Risperidone **Dosing variability:** variable	**Benefits:** ABC, CGI-S, CGI-I, discontinuation due to lack of efficacy **Harms:** Fatigue, constipation, dystonia, dyskinesia, nausea, seizure, agitation, weight	The safety and efficacy of aripiprazole and risperidone were comparable. The choice between these two medications should be on the basis of clinical equipoise considering the patient's preference and clinical profile.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	or uncontrolled medical conditions such as hypothyroidism, diabetes or cancer, (2) history of drug or alcohol abuse, (3) could not have received risperidone or aripiprazole during at least 2 wk before entering this trial, (4) could not have received additional behavioural interventions above the regular educational programming during this trial	**Caucasian %:** NR **Diagnostic breakdown (n):** see below **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** NR **Overall diagnostic breakdown (n):** Autism (38), Asperger disorder (8), PDD-NOS (9), childhood disruptive behavior disorder (1)	**Target dose (mg/day):** 2 (<40 kg), 3 (>40kg) **Daily dose (mg/day), mean±SD (range):** 1.12 **Concurrent treatments:** NR		
Ghanizadeh et al., 2014b [31] **Country:** Iran **Condition category:** Tic disorders **Funding:** Non-industry **Risk of Bias:** High (subjective), High (objective)	**Recruitment Dates:** NR **Study design:** RCT (parallel) **Diagnostic criteria:** DSM-IV-TR **Setting:** outpatient **Inclusion criteria:** 6-18 yr, primary diagnosis of tic disorder **Exclusion criteria:** Current mood disorders, psychotic symptoms, PDD, substance-related disorder, severe uncontrolled medical conditions such as	**Enrolled:** 60 **Analyzed:** 60 **Completed:** 35 **GROUP 1:** **N:**31 **Age, mean±SD (range):**11.12±3.3 yr **Males %:** 82.8 **Caucasian %:**NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** NR **GROUP 2:** **N:** 29 **Age, mean±SD (range):** 10.22±2.3 yr **Males %:** 86.2 **Caucasian %:** NR	**Treatment duration:** 8 weeks **Run-in phase:** Unclear **Run-in phase duration:** 2 weeks **Permitted drugs:** Nortriptyline, Biperiden, Citalopram, Clonidine, Fluvoxamine, Propanolol, Methylphenidate **Prohibited drugs:** NR **GROUP 1** **Drug name:** Aripiprazole **Dosing variability:** Variable **Target dose (mg/day):** 15mg/day **Daily dose (mg/day), mean±SD (range):** 4.0±2.4 mg/day **Concurrent treatments:** Nortripyline (1), Citalopram (1), Clonidine + fluvoxamine + propranolol (1), Methylphenidate (2) **GROUP 2:** **Drug name:** Risperidone	**Benefits:** YGTSS, PedsQL, ADHD RS-IV **Harms:** Neuromotor effects, metabolic effects, somnolence, exercise intollerance	Aripiprazole decreased tic scores as much as risperidone in children and adolescents with tic disorder. However this should not be interpreted as arapiprazole and risperidone being equivalent. Efficacsy and safety of other doses of these medications are recommended. Long term use of the medications needs further studies.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	neurological problems, diabetes, epilepsy, Huntington's chorea, reported cardiac problems, or clinically estimated mental retardation	**Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** NR	**Dosing variability:** Variable **Target dose (mg/day):** 3mg/day **Daily dose (mg/day), mean±SD (range):** 0.6±0.2 mg/day **Concurrent treatments:** Nortriptyline (1), Biperiden (1), Clonidine (1), Methylphenidate (2)		
Gilbert et al., 2004 [32] **Country:** USA **Condition category:** Tic disorders **Funding:** Industry, Government **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** NR **Study design:** RCT (crossover) **Setting:** NR **Diagnostic criteria:** DSM-IV-TR, clinical assessment **Inclusion criteria:** (1) 7–17 yr, (2) Tourette syndrome or chronic motor tic disorder, (3) CGI tic severity score >4 after 2 wk with no medication **Exclusion criteria:** (1) transient tic disorder, anorexia nervosa, PDD, substance/alcohol abuse or dependence within the past yr, or any psychotic disorder, (2) serious or unstable medical illness or abnormal ECG or laboratory findings, (3) sexually active females of childbearing	**Enrolled:** 19 **Analyzed:** NR **Completed:** 13 **GROUP 1** **N:** 19 (crossover) **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown (n):** Tourette syndrome (16), Chronic tic disorder (3) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (7), **c**onduct disorder (1), learning disorder (3), OCD (2), oppositional defiant disorder (2) **GROUP 2** **N:** 19 (crossover) **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown (n):** See group 1 **Treatment naïve (n):** NR **Inpatients (n):** NR	**Treatment duration:** 8 wk **Run-in phase:** Yes **Run-in phase duration:** 2 wk **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Pimozide **Dosing variability:** variable **Target dose (mg/day):** 4 **Daily dose (mg/day), mean±SD (range):** 2.4 (1–4) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** 4 **Daily dose (mg/day), mean±SD (range):** 2.5 (1–4) **Concurrent treatments:** NR	**Benefits:** CGI-I, TSSR, YGTSS **Harms:** EPS (ESRS), ECG changes, weight changes	Risperidone was superior to pimozide for tic suppression but it induced weight gain.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	potential not using contraceptives	**First episode psychosis (n):** NR **Comorbidities:** see group 1			
Gothelf et al., 2002 [109] **Country:** Israel **Condition category:** Schizophrenia and related **Funding:** Government **Newcastle-Ottawa Scale:** 3/8 stars	**Recruitment dates:** NR **Study design:** Prospective cohort (NR) **Setting:** Inpatient **Diagnostic criteria:** DSM-IV, K-SADS **Inclusion criteria:** NR **Exclusion criteria:** (1) taking medications that affect weight	**Enrolled:** 20 **Analyzed:** NR **Completed:** NR **GROUP 1** **N:** 10 **Age, mean±SD (range):** 17.0±1.6 **Males %:** 100 **Caucasian %:** NR **Treatment naïve (n):** ND **Inpatients (n):** all **First episode psychosis (n):** NR **GROUP 2** **N:** 10 **Age, mean±SD (range):** 17±1.6 **Males %:** 100 **Caucasian %:** NR **Treatment naïve (n):** 1 **Inpatients (n):** all **First episode psychosis (n):** NR	**Treatment duration:** 4 wk **Run-in phase:** Yes **Run-in phase duration:** 17.6 day (mean) **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Haloperidol **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 6.5±3.4 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 14±4.1 **Concurrent treatments:** NR	**Benefits:** NR **Harms:** Abdominal circumference, BMI, weight	Body mass index significantly increased in adolescent male inpatients treated with olanzapine but not in those given haloperidol.
Gulisano et al., 2011 [33] **Country:** Italy **Condition category:** Tic disorders **Funding:** Non-industry **Risk of Bias:** NA	**Recruitment Dates:** NR **Study design:** NRCT (parallel) **Diagnostic criteria:** DSM-IV-TR **Setting:** NR **Inclusion criteria:** With TS, 6-18 yr,	**Enrolled:** 50 **Analyzed:** 50 **Completed:** 50 **GROUP 1:** **N:**25 **Age, mean±SD (range):** 13.1±2.3 yr **Males %:** 84 **Caucasian %:** NR **Diagnostic breakdown (n):** Tourette syndrome (25)	**Treatment duration:** 24 mo **Run-in phase:** Yes **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Arapiprazole **Dosing variability:** Variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD**	**Benefits:** NR **Harms:** HR, BP, QTc	At equivalent doses, arapiprazole is characterized by a safer cardiovascular profile than pimozide, being associated with a lower frequency of QTc prolongation.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
(subjective), Medium (objective)	normal IQ **Exclusion criteria:** Patient or family history of cardiovascular symptoms	**Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** ADHD (15), OCD (11) **GROUP 2:** **N:**25 **Age, mean±SD (range):** 9.1±2.9 yr **Males %:** 88 **Caucasian %:** NR **Diagnostic breakdown (n):** Tourette syndrome (25) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** ADHD (13), OCD (13)	**(range):** 5.3±2.4 **Concurrent treatments:** NR **GROUP 2:** **Drug name:** Pimozide **Dosing variability:** Variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 4.4±1.5 **Concurrent treatments:** NR		
Haas et al., 2009b [35] **Country:** India, Russia, Ukraine, USA **Condition category:** Schizophrenia and related **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** Aug 2004 to Dec 2005 **Study design:** RCT (parallel) **Setting:** Inpatient/outpatient **Diagnostic criteria:** DSM-IV, K-SADS-PL **Inclusion criteria:** (1) male and females, (2) aged 13 to 17 years, (3) DSM-IV diagnosis of schizophrenia, (4) inpatients or outpatients,	**Enrolled:** 160 **Analyzed:** 158 **Completed:** 125 **GROUP 1** **N:** 55 **Age, mean±SD (range):** 15.7±1.3 **Males %:** 55 **Caucasian %:** 60 **Diagnostic breakdown (n):** Paranoid (38), Undifferentiated (8), Disorganized (8), Catatonic (1), Residual (0) **Treatment naïve (n):** NR **Inpatients (n):** 30 **First episode psychosis (n):** NR	**Treatment duration:** 6 wk **Run–in phase:** Yes **Run–in phase duration:** ≤5 day **Permitted drugs:** Propanolol was allowed for treatment-emergent akathisia. Antiparkinsonian medications could be initiated for treatment-emergent EPS. Use of all rescue medications was kept to a minimum, and the permitted doses of certain medications progressively decreased over the course of the study. Subjects could receive limited supportive psychotherapy or psychoeducation. **Prohibited drugs:** antidepressants, mood stabilizers, anticonvulsants,	**Benefits:** CGAS, CGI-I, CGI-S, PANSS, response, suicide **Harms:** SAS, BAS, AIMS, Behavioral issues, BMI, EPS, glucose-related AE, mortality, prolactin, prolactin-related AE, SAE, somnolence, tachycardia, tardive dyskinesia, total AE, WAE, weight change	Risperidone treatment for 6-weeks was safe and effective at daily doses of 1–3 and 4–6 mg in adolescents experiencing acute exacerbations of schizophrenia

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	experiencing an acute episode with a total PANSS score of 60 to 120 (inclusive), (5) no serious illnesses or neurological conditions, (6) females were required to a have negative pregnancy test and to be using an acceptable form of contraception. **Exclusion criteria:** (1) DSM-IV criteria for dissociative disorder, bipolar disorder, MDD, schizoaffective disorder, schizophreniform disorder, autistic disorder, or primary substance-induced psychotic disorder at screening, (2) MR (IQ<70), (3) substance dependence diagnosed by DSM-IV criteria in 3 months preceding screening, (4) significant risk of suicide or violent behavior, (5) failed to respond to adequate treatment with >2 antipsychotic drugs during the current psychotic episode, (6) hypersensitivity or intolerance to risperidone, (7) history of neuroleptic	**Comorbidities:** NR **GROUP 2** **N:** 51 **Age, mean±SD (range):** 15.7±1.3 **Males %:** 73 **Caucasian %:** 47 **Diagnostic breakdown (n):** Paranoid (34), Undifferentiated (13), Disorganized (4), Catatonic (0), Residual (0) **Treatment naïve (n):** NR **Inpatients (n):** 25 **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 3** **N:** 54 **Age, mean±SD (range):** 15.5±1.4 **Males %:** 65 **Caucasian %: 50** **Diagnostic breakdown (n):** Paranoid (38), Undifferentiated (12), Disorganized (3), Catatonic (0), Residual (1) **Treatment naïve (n):** NR **Inpatients (n):** 23 **First episode psychosis (n):** NR **Comorbidities:** NR	psychostimulants, direct dopamine agonists, cholinesterase inhibitors, herbal or over-the-counter medications with psychotripic properties, or antipsychotic other than the study medication. Drugs with sedative, hypnotic, or anxiolytic properties were not allowed, with some exceptions. Subjects were not permitted to receive insight-oriented or cognitive-behavioral psychotherapy. **GROUP 1** **Drug name:** Risperidone (low) **Dosing variability:** fixed **Target dose (mg/day):** 1–3 **Daily dose (mg/day), mean±SD (range):** NR (1–3) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Risperidone (high) **Dosing variability:** fixed **Target dose (mg/day):** 4–6 **Daily dose (mg/day), mean±SD (range):** NR (4–6) **Concurrent treatments:** NR **GROUP 3** **Drug name:** Placebo **Dosing variability:** fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR		

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	malignant syndrome or any severe drug allergy,				
Haas et al., 2009c[36] **Country:** USA **Condition category:** Bipolar (manic, mixed) **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** Dec 2003 to Dec 2005 **Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV, K-SADS-PL **Inclusion criteria:** (1) 10–17 yr, (2) medically stable, (3) acute manic/mixed episode (K-SADS-PL), (4) total score ≥20 at screening and baseline on YMRS, (5) responsible caregiver **Exclusion criteria:** (1) known intellectual impairment	**Enrolled:** 170 **Analyzed:** 169 **Completed:** 137 **GROUP 1** **N:** 50 **Age, mean±SD (range):** NR (10–17) **Males %:** 56 **Caucasian %:** 70 **Diagnostic breakdown (n):** manic episode (20), mixed episode (30) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (25), DBD (27) **GROUP 2** **N:** 61 **Age, mean±SD (range):** NR (10–17) **Males %:** 43 **Caucasian %:** 82 **Diagnostic breakdown (n):** manic episode (21), mixed episode (40) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (33), DBD (40) **GROUP 3** **N:** 58 **Age, mean±SD (range):**	**Treatment duration:** 3 wk **Run-in phase:** Yes **Run-in phase duration:** ≤5 day **Permitted drugs:** medication for EPS; sedatives/hypnotics (run-in and wk 1 only) **Prohibited drugs:** anticonvulsants, antidepressants, antimanic medications, other antipsychotics (including herbal substances); methylphenidate/other medication for ADHD **GROUP 1** **Drug name:** Risperidone (low) **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** (0.5–2.5) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Risperidone (high) **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 3 (26%), 4 (19%), 5 (15%), 6 (41%) (3–6) **Concurrent treatments:** NR **GROUP 3** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	**Benefits:** BPRS, CGI-BP, YMRS, Medication adherence, response, suicide **Harms:** Behavioral issues, BMI, dermatologic AE, EPS (AIMS, BAS, SAS), fatigue, glucose, lipid profile, mortality, prolactin, prolactin-related AE, SAE, sedation, somnolence, tardive dyskinesia, total AE, WAE, weight change	A significant reduction in manic symptoms was seen in youth when treated with risperidone (0.5–2.5 mg/d or 3–6 mg/d) compared to placebo.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		NR (10–17) **Males %:** 48 **Caucasian %:** 78 **Diagnostic breakdown (n):** manic episode (19), mixed episode (39) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (27), DBD (34)			
Haas et al., 2009a [34] **Country:** Belgium, Bulgaria, Czech Republic, Estonia, Germany, Poland, Romania, USA **Condition category:** Schizophrenia and related **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** Apr 2001 to Mar 2006 **Study design:** RCT (parallel) **Setting:** Inpatient **Diagnostic criteria:** DSM-IV, K-SADS-PL **Inclusion criteria:** (1) 13–17 yr, (2) schizophrenia, (3) currently hospitalized for an acute episode (PANSS total score 60–120) **Exclusion criteria:** (1) significant risk for suicidal or violent behavior, (2) history of NMS, tardative dyskinesia, or a known or suspected seizure disorder, (3) BMI <5th percentile or >95th percentile, (4) schizophreniform	**Enrolled:** 257 **Analyzed:** 255 **Completed:** 172 **GROUP 1** **N:** 132 **Age, mean±SD (range):** 15.6±1.32 (13–17) **Males %:** 61 **Caucasian %:** 85 **Diagnostic breakdown (n):** catatonic (3), disorganized (6), paranoid (92), residual (7), undifferentiated (24) **Treatment naïve (n):** NR **Inpatients (n):** all **First episode psychosis (n):** NR **GROUP 2** **N:** 125 **Age, mean±SD (range):** 15.6±1.25 (13–17) **Males %:** 52 **Caucasian %:** 85 **Diagnostic breakdown (n):** catatonic (4), disorganized (13), paranoid (83), residual (0),	**Treatment duration:** 8 wk **Run-in phase:** Yes **Run-in phase duration:** ≥7 day **Permitted drugs:** antiparkinsonian medications (first 3 wk), propranolol, rescue medications (diazepam, hydroxyzine, lorazepam, zolpidem, zopiclone) **Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone (low) **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 0.4 (0.2–0.6) **Concurrent treatments:** all groups: rescue medication (133) **GROUP 2** **Drug name:** Risperidone (high) **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 4 (1.5–6) **Concurrent treatments:** see group 1	**Benefits:** CGI-I, CGI-S, PANSS, medication adherence, response, suicide **Harms:** SAS, BAS, AIMS, Akathisia, behavioral issues, dyskinesia, dystonia, ECG changes, EPS, glucose, mortality, prolactin, prolactin-related AE, SAE, somnolence, tachycardia, total AE, WAE, weight change	A greater improvement in total PANSS score was found with high dose risperidone than with low dose risperidone.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	disorder	undifferentiated (25) **Treatment naïve (n):** NR **Inpatients (n):** all **First episode psychosis (n):** NR			

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Hagman et al., 2011 [37] **Country:** USA **Condition category:** Eating disorders **Funding:** Non-industry **ROB:** Medium (subjective), Medium (objective)	**Recruitment dates:** Aug 2004 to Sept 2008 **Study design:** RCT (parallel) **Setting:** Inpatient/outpatient **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) primary diagnosis of AN, (2) female gender, (3) 12-21 yr, (4) active in a level of care in the eating disorders program **Exclusion criteria:** (1) previous enrollment in study, (2) allergic reaction to risperidone or another atypical neuroleptic drug, (3) a positive pregnancy test result, (4) taking a psychotropic medication other than an antidepressant, (5) active hepatic or renal disease, (6) male gender, (7) wards of court	**Enrolled:** 41 **Analyzed:** 40 **Completed:** 40 **GROUP 1** **N:** 18 **Age, mean±SD (range):** 16.2±(2.5) yr **Males %:** 0 **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** depression (NR), obsessive-compulsive disorder (NR), anxiety disorder (NR), bulimia nervosa (NR) **GROUP 2** **N:** 22 **Age, mean±SD (range):** 15.8±(2.3) yr **Males %:** 0 **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** see group 1	**Treatment duration:** 9 wk **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** antidepressants (if on stable dose for >1 wk before entering the study, no dose adjustments during study), multivitamin, zinc, medications for other medical conditions (constipation, asthma, gastritis) **Prohibited drugs:** new psychotropic medications **GROUP 1** **Drug name:** Risperidone **Dosing variability:** flexible **Target dose (mg/day):** 4.0 **Daily dose (mg/day), mean±SD (range):** 2.5±1.2 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo **Dosing variability:** flexible **Target dose (mg/day):** 4.0 **Daily dose (mg/day), mean±SD (range):** 3.0±1.0 **Concurrent treatments:** NR	**Benefits:** EDI-2 DT, EDI-2 BD, ADJ-current, ADJ-desired, CAPT, MASC, suicidal ideation, anxiety, depression **Harms:** EPS (AIMS, SAS), glucose, lipid profile, prolactin, fatigue, blood pressure	This exploratory pilot study does not demonstrate a clear benefit from the addition of risperidone in the course of active treatment and weight restoration in adolescents with AN.
Hellings et al., 2006 [38] **Country:** USA	**Recruitment dates:** NR **Study design:** RCT	**Enrolled:** 26 **Analyzed:** 26 **Completed:** NR	**Treatment duration:** 5.1 mo (6 wk at each dose) **Run-in phase:** Yes	**Benefits:** ABC, CGI-I, PAC, VAS **Harms:** NMS, tardive	Compared to placebo, risperidone was more effective in treating

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Condition category: ASD **Funding:** Industry, Government **Risk of bias:** High (subjective), High (objective)	(crossover) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) 6–65 yr, (2) MR (IQ <70), (3) at least 6 mo history of aggression, property destruction, or self-injury, (4) above normal baseline Irritability score for age, gender and setting (ABC-C) **Exclusion criteria:** (1) previous risperidone hypersensitivity, (2) history of NMS, (3) seizures within the past yr, (4) degenerative brain disease, (5) problematic living situation	**GROUP 1** **N:** 26 (crossover) **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** Autistic Disorder (ND), MR (Mild (8), moderate (6), severe (8), profound (4)), PDD-NOS (ND) **GROUP 2** **N:** 26 (crossover) **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** see group 1 **GROUP 3** **N:** 26 (crossover) **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** see group 1	**Run-in phase duration:** 5–7 wk **Permitted drugs:** divalproex, gabapentin (if epilepsy was in remission ≥1 yr) **Prohibited drugs:** psychotropics, including stimulants **GROUP 1** **Drug name:** Risperidone (low) **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** all groups: divalproex (5), gabapentin (1) **GROUP 2** **Drug name:** Risperidone (high) **Dosing variability:** variable **Target dose (mg/day):** 0.05 mg/kg/day **Daily dose (mg/day), mean±SD (range):** 2 (1.2–2.9) **Concurrent treatments:** see group 1 **GROUP 3** **Drug name:** Placebo II **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** see group 1	dyskinesia, weight change	problematic behaviors in children and adolescents with MR. Low doses were better tolerated and were equally effective compared to high doses.
Hollander et al.,	**Recruitment dates:**	**Enrolled:** 11	**Treatment duration:** 8 wk	**Benefits:** CGI-I,	Olazapine improved

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
2006 [39] **Country:** USA **Condition category:** ASD **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	NR **Study design:** RCT (parallel) **Setting:** NR **Diagnostic criteria:** DSM-IV, ADI-R, ADOS **Inclusion criteria:** (1) 6–17 yr, (2) meets DSM-IV and ADI-R criteria with a rating of at least moderate (≥4) on the CGI **Exclusion criteria:** (1) response to prior pharmacological treatment, (2) psychotic disorders and a history of any clinically significant medical illness (with the exception of a stable seizure disorder)	**Analyzed:** 11 **Completed:** 8 **GROUP 1** **N:** 6 **Age, mean±SD (range):** 9.3±2.9 (6–14.8) **Males %:** 100 **Caucasian %:** 50 **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (normal (2), mild (2), severe (2)) **GROUP 2** **N:** 5 **Age, mean±SD (range):** 8.9±2.1 (6.1–11) **Males %:** 60 **Caucasian %:** 80 **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (normal (2), mild (3))	**Run-in phase:** Yes **Run-in phase duration:** 4 wk **Permitted drugs:** anticonvulsants (stable dose ≥3 mo), clonidine, chloral hydrate **Prohibited drugs:** NR **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 10±2 (7.5–12.5) **Concurrent treatments:** none **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 10±2 (7.5–12.5) **Concurrent treatments:** none	response (CGI-I, CPRS) **Harms:** Constipation, EPS (AIMS, BAS, SAS), sedation, weight change	global functioning in children and adolescents with PDD, but was associated with a significant risk of weight gain.
Hrdlicka et al., 2009 [110] **Country:** Czech Republic **Condition category:** Schizophrenia and related **Funding:** Government,	**Recruitment dates:** 1997 to 2007 **Study design:** Retrospective cohort **Setting:** Inpatient **Diagnostic criteria:** ICD-10 **Inclusion criteria:** (1) schizophrenia dx (F20-	**Enrolled:** 109 **Analyzed:** NR **Completed:** 52 **GROUP 1** **N:** 24 **Age, mean±SD (range):** 15.8±1.6yr (all) **Males %:** 48% (all) **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis**	**Treatment duration:** 6 wk **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Typical (Haloperidol, Perphenazine, Sulpiride) **Dosing variability:** variable **Target dose (mg/day):** NR	**Benefits:** NR **Harms:** Weight changes	Weight gain did not differ between the groups on typical and atypical antipsychotics.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Academic **Newcastle-Ottawa Scale:** 5/8 stars	29), (2) medical record quality sufficient to evaluate the patient, (3) the first treatment used following admission was considered (with the exception of clozapine), (4) only antipsychotic treatments initiated after admission to the Department of Child Psychiatry were analyzed **Exclusion criteria:** NR	**(n):** NR **GROUP 2** **N:** 85 **Age, mean±SD (range):** see above **Males %:** see above **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR	**Daily dose (mg/day), mean±SD (range):** Haloperidol 6.8±1.1, Perphenazine 12±6.9, Sulpiride 450±409.3 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Atypical (Clozapine, Olanzapine, Risperidone, Ziprasidone) **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** Clozapine 247.5±118, Olanzapine 15±6.1, Risperidone 2.7±1.3, Ziprasidone 80±0 **Concurrent treatments:** NR		
Jensen et al., 2008 [40] **Country:** USA **Condition category:** Schizophrenia and related **Funding:** NR **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** May 2003 to June 2006 **Study design:** RCT (parallel) **Setting:** Inpatient (most) **Diagnostic criteria:** DSM-IV, K-SADS **Inclusion criteria:** (1) 10–18 yr, (2) schizophrenia/ schizoaffective disorder, schizophreniform, or psychotic disorder NOS, (3) ≥1 positive or negative symptom associated with schizophrenia present	**Enrolled:** 30 **Analyzed:** 29 **Completed:** 21 **GROUP 1** **N:** 10 **Age, mean±SD (range):** 15.3±1.5 **Males %:** 50 **Caucasian %:** 50 **Diagnostic breakdown (n):** psychotic disorder NOS (6), schizophrenia, schizoaffective, schizophreniform disorder (4) **Treatment naïve (n):** NR **Inpatients (n):** 9 **First episode psychosis (n):** NR **Comorbidities:** MR (0), psychosis (all) **GROUP 2**	**Treatment duration:** 2.8 mo **Run-in phase:** Yes **Run-in phase duration:** 2 wk **Permitted drugs:** diphenhydramine (≤100 mg/day), lorazepam (0.5–2 mg/day) **Prohibited drugs:** antidepressants, mood stabilizers, and stimulants (discontinued prior to or within first 2 wk of trial) **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** 20 **Daily dose (mg/day), mean±SD (range):** 14±4.6 (5–20) **Concurrent treatments:** anticholinergics (0), dietary counselling, psychoeducation **GROUP 2**	**Benefits:** PANSS, CGAS, CGI-S, medication adherence, response **Harms:** AIMS, SAS, akathisia, behavioral issues, dyskinesia, EPS, mastitis, sedation, WAE, weight change	There was no statistically significant difference between groups in the reduction of PANSS scores; however a larger RCT may be warranted to test the clinical significance of differences between treatment with quetiapine and risperidone.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	throughout the past 2 wk (PANSS) **Exclusion criteria:** (1) MR or affective disorder with psychotic features, (2) current alcohol or drug dependence or abuse, (3) history of serious adverse reactions or nonresponse to an adequate trial of any of the proposed treatments, (4) pregnant or refusal to practice contraception, (5) serious and unstable medical condition	**N:** 10 **Age, mean±SD (range):** 14.8±2.3 **Males %:** 70 **Caucasian %:** 60 **Diagnostic breakdown (n):** psychotic disorder NOS (3), schizophrenia, schizoaffective, schizophreniform disorder (7) **Treatment naïve (n):** NR **Inpatients (n):** 9 **First episode psychosis (n):** NR **Comorbidities:** MR (0), psychosis (all) **GROUP 3** **N:** 10 **Age, mean±SD (range):** 15.6±2.5 **Males %:** 80 **Caucasian %:** 70 **Diagnostic breakdown (n):** psychotic disorder NOS (0), schizophrenia, schizoaffective, schizophreniform disorder (10) **Treatment naïve (n):** NR **Inpatients (n):** 9 **First episode psychosis (n):** NR **Comorbidities:** MR (0), psychosis (all)	**Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** 800 **Daily dose (mg/day), mean±SD (range):** 611±253.4 (100–800) **Concurrent treatments:** anticholinergics (0), dietary counselling, psychoeducation **GROUP 3** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** 6 **Daily dose (mg/day), mean±SD (range):** 3.4±1.5 (1–6) **Concurrent treatments:** anticholinergics (0), dietary counselling, psychoeducation,		
Jerrell et al., 2008[111] **Country:** USA **Condition**	**Recruitment dates:** Jan 1996 to Dec 2005 **Study design:** Retrospective	**Enrolled:** NA **Analyzed:** 4140 **Completed:** 4140 **GROUP 1** **N:** 4140	**Treatment duration:** ≥9 mo **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** NR	**Benefits:** NR **Harms:** Weight gain, type 2 diabetes mellitus, dyslipidemia, hypertension,	When evaluating the overall benefit-risk ratio of all psychotropics prescribed in

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
category: Mixed **Questions:** KQ2, KQ3 **Funding:** Non-industry **Newcastle-Ottawa Scale:** 6/8 stars	**Setting:** Inpatient/ outpatient **Diagnostic criteria:** ICD-9-CM **Inclusion criteria:** (1) Child and adolescent pateints, (2) ≤17 yr, (3) enrolled in and eligible for Medicaid for ≥ 9 mo in each calendar year, (4) who had a service encounter, (5) who were prescribed 1 of 5 atypical (aripiprazole, ziprasidone, quetiapine, risperidone, olanzapine) or 2 conventional antipsychotics (haloperidol or fluphenazine) **Exclusion criteria:** NR	**Age, mean±SD (range):** NR **Males %:** 68 **Caucasian %:** 42 **Diagnostic breakdown (n):** Schizophrenia or other psychotic disorders (1507), major affective disorders (2261), ADHD (3258) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** Epilepsy (954), CNS disorders (919), organic brain syndrome or severe MR (704), congenital heart defects (146), endocrine disorder (168), preexisting obesity (680), preexisting type II diabetes mellitus or dyslipidemia (404), preexisting cardiovascular disorder (246)	**Prohibited drugs:** NR **GROUP 1** **Drug name:** Antipsychotics cohort **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 7.4±3.1 **Concurrent treatments:** SSRI (2367), , weight-inducing antidepressants (3292), psychostimulants (3170), multiple antipsychotics (1756), mood stabilizers (1898)	cardiovascular/ cerebrovascular events, orthostatic hypotension/ syncope, EPS, seizures, sedation/ somnolence, sexual/ reproductive	children and adolescents, the practitioner needs to give careful consideration to possible toxicities that have been previously demonstrated in this and other studies, especially in individuals receiving concomitant psychotropic medications, and to children with preexisting/comorbid medical conditions or diet/family risk factors that might increase their potential for experiencing adverse reactions.
Johnson & Johnson, 2011 [41] **Country:** NR **Condition category:** Schizophrenia and related **Funding:** Industry **Risk of bias:** High (subjective), High	**Recruitment dates:** Mar to Aug 2006 **Study design:** RCT (parallel) **Setting:** NR **Diagnostic criteria:** DSM-IV-TR **Inclusion criteria:** (1) male or female, (2) aged 10 to 17 years,	**Enrolled:** 25 **Analyzed:** 25 **Completed:** 24 **GROUP 1** **N:** 8 **Age, mean±SD (range):** all groups: 14.6±2.2 (10–17) **Males %:** all groups: 72 **Caucasian %:** all groups: 56 **Diagnostic breakdown (n):** all groups:	**Treatment duration:** 7 days **Run–in phase:** Yes **Run–in phase duration:** 21 days maximum **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Paliperidone ER **Dosing variability:** fixed **Target dose (mg/day):** 0.086 mg/kg/day	**Benefits:** NR **Harms:** total AE, serious AEs, mortality, prolactin, prolactin-related AE, orthostatic hypotension, ECG changes, EPS scales	Pediatric subjects tolerated doses from 4 to 12 mg paliperidone ER (corresponding to weight-adjusted doses ranging from 0.086 and 0.171 mg/kg).

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
(objective)	(3) height and weight within the 5th to 95th percentile for age and sex, (4) DSM-IV-TR diagnosis of schizophrenia of any subtype, schizoaffective or schizophreniform (3) otherwise healthy, (4) CGI-S score of =< 3 **Exclusion criteria:** NR	schizophreniform disorder (8), schizoaffective disorder (7), paranoid (6), undifferentiated (3), disorganized (1) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 2** **N:** 9 **Age, mean±SD (range):** see group 1 **Males %:** see group 1 **Caucasian %:** see group 1 **Diagnostic breakdown (n):** see group 1 **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 3** **N:** 8 **Age, mean±SD (range):** see group 1 **Males %:** see group 1 **Caucasian %:** see group 1 **Diagnostic breakdown (n):** see group 1 **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR	**Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 2** **Drug name:** Paliperidone ER **Dosing variability:** fixed **Target dose (mg/day):** 0.129 mg/kg/day **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 3** **Drug name:** Paliperidone ER **Dosing variability:** fixed **Target dose (mg/day):** 0.171 mg/kg/day **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR		
Kafantaris et al., 2011 [42] **Country:** USA	**Recruitment dates:** NR **Study design:** RCT (parallel)	**Enrolled:** 20 **Analyzed:** 20 **Completed:** 15 **GROUP 1**	**Treatment duration:** 10 wk **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** NR	**Benefits:** HDRS, Brief Psychiatric Rating Scale, EDE, YBC-EDS, medication	The lack of support for olanzapine's efficacy relative to placebo in the context of our

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Condition category: Eating disorders **Funding:** Industry **ROB:** Medium (subjective), Medium (objective)	**Setting:** Inpatient/outpatient **Diagnostic criteria:** EDE (Eating Disorder Examination) **Inclusion criteria:** (1) females who received treatment for AN at the Eating Disorder Treatment Program over a 4 yr period, (2) between 12-21 yr, (3) primary diagnosis of ANR **Exclusion criteria:** (1) past or current binge/purge type, (2) serious suicidal risk, (3) prior treatment with olanzapine, (4) not on a sable medication regimen for 8 wk prior to study entry	**N:** 10 **Age, mean±SD (range):** 16.4±2.2 yr **Males %:** 0 **Caucasian %:** see below **Diagnostic breakdown (n):** NR **Treatment naïve (n):** 10 **Inpatients (n):** see below **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 10 **Age, mean±SD (range):** 18.1±2.0 yr **Males %:** 0 **Caucasian %:** see below **Diagnostic breakdown (n):** NR **Treatment naïve (n):** 10 **Inpatients (n):** see below **First episode psychosis (n):** NR **Comorbidities:** NR **Overall Caucasian %:** 80 **Overall inpatients (n):** 9	**Prohibited drugs:** NR **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** flexible **Target dose (mg/day):** 10 **Daily dose (mg/day), mean±SD (range):** NR (started with 2.5mg single oral dose; increased by 2.5mg each wk to reach target dose) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo **Dosing variability:** flexible **Target dose (mg/day):** 10 **Daily dose (mg/day), mean±SD (range):** NR (started with 2.5mg single oral dose; increased by 2.5mg each wk to reach target dose) **Concurrent treatments:** NR	adherence **Harms:** dystonia, akathisia, dyskinesia, weight gain (BMI), glucose, insulin, cardiac function	comprehensive treatment setting, coupled with concerns regarding increases in insulin and glucose, dissuaded us from pursuing a larger placebo-controlled study of adjunctive olanzapine for adolescents with AN-R at our setting.
Kent et al., 2013 [43] **Country:** USA **Condition category:** ASD **Funding:** Industry **Risk of bias:** Medium (subjective),	**Recruitment dates:** Dec 2007 to Mar 2010 **Study design:** RCT (parallel) **Setting:** NR **Diagnostic criteria:** DSM-IV-TR, ADI-R **Inclusion criteria:** (1)	**Enrolled:** 96 **Analyzed:** 96 **Completed:** 77 **GROUP 1** **N:** 30 **Age, mean±SD (range):** NR **Males %:** 83 **Caucasian %:** 70 **Diagnostic breakdown (n):** autistic disorder (all)	**Treatment duration:** 6 wk **Run–in phase:** Yes **Run–in phase duration:** 3 wk **Permitted drugs:** Anticholinergics, antihistamine, hypnotic, sedative (lorazepam, diphenhydramine) **Prohibited drugs:** Psychotropic medications for atleast 1 week (4 weeks for fluoxetine, 8 weeks for depot medications)	**Benefits:** ABC-I, ABC (other sub scales), CGI-S, CYBOCS, CGI-I, response, aggression **Harms:** EPS (AIMS, BAS, SAS) Somnolence, weight increase (BMI), mortality, akathisia, tardive dyskinesia,	Data from this study demonstrate that risperidone at higher doses of 1.25 and 1.75 mg/day were efficacious; however, risperidone at doses <0.25 mg did not demonstrate significant efficacy in the treatment of

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Medium (objective)	Male or female 5–17 years old, (2) Body weight of ≥20 kg (3) DSM-IV diagnosis of Autistic Disorder (299.00), corroborated by standard cut-off scores on the ADI-R, ABC-I Subscale score of 18 or more, CGI-S of ≥4, (4) mental age >18 months, (5) patients with history of seizures required to be seixure free for at least 6 consecutive months or on stable dosage of antiepileptic frugs ≥ 4 weeks before screening, (6) normal fasting glucose and creatinine, and liver funcion tests levels <1.5 times normal upper limit **Exclusion criteria:** (1) Previous or current DSM-IV diagnosis of psychotic disorder or PDD other than autism, (2) neurologic disorders, (3) moderate/severe extrapyramidal symptoms or tardive dyskinesia, (4) lack of response to risperidone treatment in the past, (5) pregnant/breast feeding girls	**Treatment naïve (n):** 26 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 31 **Age, mean±SD (range):** NR **Males %:** 90 **Caucasian %:** 81 **Diagnostic breakdown (n):** autistic disorder (all) **Treatment naïve (n):** 29 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 3** **N:** 35 **Age, mean±SD (range):** NR **Males %:** 89 **Caucasian %:** 60 **Diagnostic breakdown (n):** autistic disorder (all) **Treatment naïve (n):** 32 **Inpatients (n):** NR **First episode psychosis:**NR **Comorbidities:** NR	**GROUP 1** **Drug name:** Risperidone **Dosing variability:** fixed **Target dose (mg/day):** 0.125 (20<45 kg), 0.175 (≥45kg) **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** methylphenidate (1) **GROUP 2** **Drug name:** Risperidone **Dosing variability:** fixed **Target dose (mg/day):** 1.25 (20<45 kg), 1.75 (≥45kg) **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** methylphenidate (1) **GROUP 3** **Drug name:** Placebo **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** methylphen-idate (1), alprazolam (1), melatonin (2)	prolactin, prolactin-related AE (oligomenorrhea), glucose metabolism related AE, elevated insulin levels, lipid profile, nausea, ECG, constipation, agitation	irritability and related behaviors associated with autistic disorder in children and adolescents, consistent with current labeling.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Khan et al., 2009 [112] **Country:** USA **Condition category:** Mixed conditions **Funding:** NR **Newcastle-Ottawa Scale:** 6/8 stars	**Recruitment dates:** Sept 2003 to Aug 2005 **Study design:** Retrospective **Setting:** Inpatient **Diagnostic criteria:** Medical record **Inclusion criteria:** (1) <18 yr, (2) treated with olanzapine or risperidone between Sept 2003 to Aug 2005 at the child and adolescent psychiatric unit of the Austin State Hospital **Exclusion criteria:** (1) ≥18 yr, (2) who received antipsychotic polypharmacy or >2 wk of cross titration between antipsychotics, (3) who received one of the study medications within 4 wk prior to their inpatient admission or who received the study medication <2 wk during inpatient hospital stay, (4) subjects who did not have either a lipid profile or a glucose level drawn during admission	**Enrolled:** NA **Analyzed:** 49 **Completed:** 49 **GROUP 1** **N:** 25 **Age, mean±SD (range):** 13.0±3.5 yr **Males %:** 64 **Caucasian %:** 72 **Diagnostic breakdown (n):** See below **Treatment naïve (n):** NR **Inpatients (n):** 25 **First episode psychosis (n):** NR **Comorbidities:** See below **GROUP 2** **N:** 24 **Age, mean±SD (range):** 13.0±3.5 yr **Males %:** 83 **Caucasian %:** 58 **Diagnostic breakdown (n):** See below **Treatment naïve (n):** NR **Inpatients (n):** 24 **First episode psychosis (n):** NR **Comorbidities:** See below **Overall diagnostic breakdown (n):** BP (NR), mood disorder NOS (NR), major depressive disorder (NR), schizoaffective disorder, schizophrenia, and schizophreniform disorder (7)	**Treatment duration:** Olanzapine 27±12 d, risperidone 26±13 d **Run-in phase:** Yes **Run-in phase duration:** 2-4 wk **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 12.5 (range 5-25 mg) **Concurrent treatments:** Stimulants (5) **GROUP 2** **Drug name:** Risperidone **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 2.6 (range 1-7 mg) **Concurrent treatments:** Stimulants (6)	**Benefits:** NA **Harms:** BMI, systolic/ diastolic blood pressure, lipid profile, fasting glucose	Treatment with both olanzapine and risperidone results in a significant increase in BMI. Also, olanzapine significantly increases risk factors for diabetes mellitus and overall risk factors for metabolic syndrome. Clinicians should consider potential metabolic effects while selecting antipsychotics and educate patients on these effects.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Overall comorbidities: SUD (14), ADHD (8)			
Khan et al., 2006 [113] **Country:** USA **Condition category:** Mixed conditions **Funding:** NR **Newcastle-Ottawa Scale:** 4/8 stars	**Recruitment dates:** Jan 2003 to Jan 2005 **Study design:** Retrospective cohort **Setting:** Inpatient **Diagnostic criteria:** NR **Inclusion criteria:** (1) <18 yr, (2) hospitalized with any mental illness, (3) treatment with IM ziprasidone or olanzapine for acute agitation/agression, (4) hospitalized during study period **Exclusion criteria:** (1) >18 yr, (2) moderate, severe or profound MR, (3) patients who did not receive IM ziprasidone/ olanzapine for agitation or agression during their inpatient stay, (4) patients receiving both IM ziprasidone and olanzapine	**Enrolled:** NA **Analyzed:** 100 **Completed:** 100 **GROUP 1** **N:** 50 **Age, mean±SD (range):** 13.7±2.4 **Males %:** 68 **Caucasian %:** 60 **Diagnostic breakdown (n):** any Axis I dx with psychosis (18) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** PTSD (18), SA (27) **GROUP 2** **N:** 50 **Age, mean±SD (range):** 14.6±2.1 **Males %:** 32 **Caucasian %:** 68 **Diagnostic breakdown (n):** any Axis I dx with psychosis (16) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** see group 1	**Treatment duration:** Olanzapine 3.7 (2.4) wk, Ziprasidone 4.9 (3.4) wk (mean(SD)) **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** total 8.2±2.4, children 6±2.2, adolescents 9.20±1.8 **Concurrent treatments:** antipsychotic other than ziprasidone (41); aripiprazole, quetiapine most commonly prescribed **GROUP 2** **Drug name:** Ziprasidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** total 19.1±2.7, children 15.7±4.4, adolescents 19.5±2.1 **Concurrent treatments:** antipsychotics (48) (olanzapine (13), clozapine (4)); aripiprazole, quetiapine the most commonly prescribed	**Benefits:** NA **Harms:** Dermatologic AE, pseudoparkinsonism, sedation	IM ziprasidone and IM olanzapine may be equally effective for the treatment of children and adolescents with agitation and aggression.
Kowatch et al., 2015 [44]	**Recruitment dates:** Sept 2005 to Sept 2010	**Enrolled:** 25 **Analyzed:** 25 **Completed:** 23	**Treatment duration:** 6 wk **Run–in phase:** Yes **Run–in phase duration:** 4 wk	**Benefits:** YMRS, CGI-I, CDRS, response, irritability	In this small sample of preschool children with BD, risperidone

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Country: USA **Condition category:** Bipolar disorder **Funding:** Non-industry **Risk of bias:** Medium (subjective), Medium (objective)	**Study design:** RCT (parallel) **Setting:** Outpatient **Diagnostic criteria:** DSM-IV-TR, K-SADS, PAPA **Inclusion criteria:** (1) Male and female, (2) aged 3-7yr 11 mo, (3) bipolar I disorder , mixed or manic, psychotic or nonpsychotic (according to DSM-IV-TR, K-SADS [for 6-7 yr] and PAPA [for3-5 yr]), (4)) permitted to have comorbid ADHD **Exclusion criteria:** (1) Clinically significant or unstable hepatic, renal, gastroenterological, respiratory, cardiovascular, endocrine, immunological, hematological, or other systemic medical conditions, (2) neurological disorders including epilepsy, stroke, or severe head trauma, (3) clinically significant laboratory abnormalities on complete blood count (CBC) with differential, electrolytes, blood urea	**GROUP 1** **N:** 18 **Age, mean±SD (range):** 5.31±1.3 yr **Males %:** 61 **Caucasian %:** 61 **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** ADHD (37%), ODD (4.3%), GAD (8.7%) **GROUP 2** **N:** 7 **Age, mean±SD (range):** 5.19±1.0 yr **Males %:** 71 **Caucasian %:** 71 **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** ADHD (15.2%), ODD (0%), GAD (6.5%)	(aripiprazole/fluoxetine), 2 wk (other psychotropic) **Permitted drugs:** Oral chlorpromazine in low doses for sleep disturbance and agitation during the first 2 wk of trial **Prohibited drugs:** Antipsychotic, antidepressant, mood stabilizer/ anticonvulsant other than study drug **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 0.5(0.5-0.75)mg/day **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	**Harms:** EPS (AIMS, BAS, SAS), ECG, lipid profile, liver function tests, prolactin, insulin, weight (BMI), hematologic values	demonstrated clear efficacy versus placebo. Treatment with risperidone over 6 weeks led to increased prolactin levels, liver functions, metabolic measures, and weight/BMI.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	nitrogen (BUN), creatinine, hepatic transaminases, urinalysis, thyroid indices (T3, total T4, tree T4, thyroid-stimulating hormone [TSH]) and electrocardiogram (ECG), (4) mania caused by a general medical condition or substance-induced mania, (5) mental retardation (intelligence quotient [IQ] < 70); evidence of fetal alcohol syndrome or an alcohol-related neurodevelopmental disorder, (6) or schizophrenia or other psychotic disorders (including schizophreniform disorder, schizoaffective disorder, delusional disorder, brief psychotic disorder, shared psychotic disorder, psychotic disorder caused by a general medical condition, substance-induced psychotic disorder, psychotic disorder not otherwise specified) as defined in the DSM-IV				
Kryzhanovskaya et al., 2009 [45]	**Recruitment dates:** Nov 2002 to Apr 2005	**Enrolled:** 107 **Analyzed:** 107	**Treatment duration:** 6 wk **Run-in phase:** Yes	**Benefits:** BPRS-C, PANSS, CGI-I, CGI-	Adolescents with schizophrenia

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Completed: 64	**Run-in phase duration:** 2–14 day	S, OAS, medication adherence, response, suicide	experienced significant symptom improvement when treated with olanzapine compared to placebo.
Country: Russia, USA **Condition category:** Schizophrenia and related **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV-TR, K-SADS **Inclusion criteria:** (1) 13–17 yr, (2) schizophrenia (paranoid, disorganized, catatonic, undifferentiated, and residual types), (3) able to perform all protocol–required examinations, (4) total score ≥35 on the anchored version of the BPRS-C16 and a score ≥3 on at least one of the following BPRS-C items at enrolment and randomization: hallucinations, delusions, or peculiar fantasies, (5) previously treated with clozapine and other atypical antipsychotics **Exclusion criteria:** (1) previous participation in a clinical trial of oral olanzapine, (2) treatment within 30 day of the trial with a drug	**GROUP 1** **N:** 72 **Age, mean±SD (range):** 16.1±1.3 (13–18) **Males %:** 70.8 **Caucasian %:** 72.2 **Treatment naïve (n):** 21 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (0), SA (0) **GROUP 2** **N:** 35 **Age, mean±SD (range):** 16.3±1.6 (13.1–18) **Males %:** 68.6 **Caucasian %:** 71.4 **Treatment naïve (n):** 5 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (0), SA (0)	**Permitted drugs:** anticholinergics (2–6mg/day), benzodiazepines (2 mg/day lorazepam equivalents for ≤3 consecutive days) **Prohibited drugs:** NR **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 11.1 (2.5–20) **Concurrent treatments:** anticholinergics (3), benzodiazepines (21) **GROUP 2** **Drug name:** Placebo **Dosing variability:** fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** anticholinergics (2), benzodiazepines (18)	**Harm:** AIMS, BAS, SAS, BMI, ECG changes, glucose, hepatic enzyme, lipid profile, mortality, prolactin, sedation, schizophrenia, somnolence, WAE, weight change	

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	without regulatory approval for any indication, (3) documented olanzapine allergic reaction, (4) previous nonresponse to an adequate dose/duration of olanzapine treatment, (5) potential safety concerns, (6) pregnancy, nursing, or refusal to practice acceptable contraception, (7) acute/ unstable medical conditions, (8) current/expected use of any concomitant psychotropic medications (except for permitted drugs), (9) baseline prolactin ≥200 ng/mL, (10) clinically significant laboratory abnormalities, (11) DSM-IV-TR substance dependence within 30 day (except nicotine and caffeine) (12) current DSM-IV-TR dx of a comorbid psychiatric or developmental disorder				
Kumra et al., 2008[47] **Country:** USA **Condition**	**Recruitment dates:** Sep 2001 to Mar 2006 **Study design:** RCT (parallel)	**Enrolled:** 40 **Analyzed:** 39 **Completed:** 28 **GROUP 1** **N:** 19	**Treatment duration:** 2.8 mo **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** current medications tapered as tolerated	**Benefits:** BPRS, CGAS, CGI-I, CGI-S, SANS, response **Harms:** Blood cells, BMI, constipation,	A greater number of children diagnosed with schizophrenia/ schizoaffective disorder and treated with clozapine met

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
category: Schizophrenia and related **Funding:** NR **Risk of bias:** High (subjective), High (objective)	**Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV, K-SADS-PL, structured interview **Inclusion criteria:** (1) 10–18 yr, (2) schizophrenia or schizoaffective disorder, (3) treatment refractoriness (documented treatment failure of ≥2 prior adequate antipsychotic trials and a baseline BRPS total score ≥35 and at least moderate on one or more psychotic items on the BRPS) **Exclusion criteria:** (1) premorbid dx of MR, (2) history of serious adverse reactions to the proposed treatments, (3) pregnant, (4) serious and unstable medical condition, (5) failed an adequate trial of clozapine (≥12 wk) at adequate doses (≥300mg/day) and/or failed an adequate trial of olanzapine (≥8wk) at high doses (≥20mg/day)	**Age, mean±SD (range):** 15.8±2.2 **Males %:** 44.4 **Caucasian %:** 11.1 **Diagnostic breakdown (n):** schizoaffective disorder (7), schizophrenia (11) **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** 0 **Comorbidities:** MR (0) **GROUP 2** **N:** 21 **Age, mean±SD (range):** 15.5±2.1 **Males %:** 61.9 **Caucasian %:** 28.6 **Diagnostic breakdown (n):** schizoaffective disorder (7), schizophrenia (14) **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** 0 **Comorbidities:** MR (0)	(first 4 wk of trial) **Prohibited drugs:** NR **GROUP 1** **Drug name:** Clozapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 403.1±201.8 (50–700) **Concurrent treatments:** all groups: antidepressants (4), depakoate (3), lithium (7), mood stabilizer (6), naltrexone (1), stimulant (1); group 1: n=6 **GROUP 2** **Drug name:** Olanzapine (high dose) **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 26.2±6.5 (10–30) **Concurrent treatments:** see group 1; group 2: n=11	diabetes, EPS, glucose, lipid profile, prolactin, SAE, WAE, weight change	drug response criteria than children treated with olanzapine. Clinicians should be aware of potential metabolic adverse events of long-term clozapine treatment.
Kumra et al., 1998 [114]	**Recruitment dates:** NR	**Enrolled:** 23 **Analyzed:** 23	**Treatment duration:** Clozapine 6 wk, Olanzapine 8 wk	**Benefits:** BPRS, SANS, SAPS,	Preliminary data suggested clozapine

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Completed: 21	**Run-in phase:** Yes	response	and olanzapine
Country: USA	**Study design:** Prospective cohort	**GROUP 1**	**Run-in phase duration:** 17.5 day (mean)	**Harms:** Behavioral issues, blood cells, constipation, EPS, liver function, seizure, somnolence, tachycardia, weight change	were efficacious in children and adolescents with treatment-refractory schizophrenia.
Condition category: Schizophrenia and related	**Setting:** Inpatient	**N:** 15	**Permitted drugs:** benzodiazepines (<8 mg/day)		
Funding: Industry	**Diagnostic criteria:** DSM-III-TR, K-SADS-E	**Age, mean±SD (range):** 13.6±1.5	**Prohibited drugs:** NR		
Newcastle-Ottawa Scale: 5/8 stars	**Inclusion criteria:** (1) schizophrenia with psychotic symptoms documented by 12 yr (DSM-III-R), (2) failure of two prior neuroleptic treatments, (3) communication capability, (4) premorbid Full Scale IQ >70	**Males %:** 53.3	**GROUP 1**		
		Caucasian %: NR	**Drug name:** Clozapine		
		Diagnostic breakdown (n): disorganized (8), paranoid (2), undifferentiated (5)	**Dosing variability:** variable		
		Treatment naïve (n): 0	**Target dose (mg/day):** NR		
		Inpatients (n): all	**Daily dose (mg/day), mean±SD (range):** 317±147 (100–600)		
		First episode psychosis (n): 0	**Concurrent treatments:** NR		
	Exclusion criteria: (1) any significant unstable neurological or medical disorder, (2) current serious suicidal risk, (3) active alcohol or drug abuse	**GROUP 2**	**GROUP 2**		
		N: 8	**Drug name:** Olanzapine		
		Age, mean±SD (range): 15.3±2.3	**Dosing variability:** variable		
		Males %: 50	**Target dose (mg/day):** NR		
		Caucasian %: NR	**Daily dose (mg/day), mean±SD (range):** 17.5±2.3 (12.5–20)		
		Diagnostic breakdown (n): disorganized (3), paranoid (1), undifferentiated (4)	**Concurrent treatments:** benzodiazepines (7), lithium (1)		
		Treatment naïve (n): 0			
		Inpatients (n): all			
		First episode psychosis (n): 0			
Kumra et al., 1996 [46]	**Recruitment dates:** NR	**Enrolled:** 21	**Treatment duration:** 6 wk	**Benefits:** BPRS-C, CGAS, CGI-I, SANS, SAPS,	Clozapine was more effective in controlling positive and negative symptoms in treatment-refractory childhood onset schizophrenia than haloperidol.
		Analyzed: 21	**Run-in phase:** Yes		
		Completed: 17	**Run-in phase duration:** 6 wk		
Country: USA	**Study design:** RCT (parallel)	**GROUP 1**	**Permitted drugs:** group 1: benztropine mesylate (≤6 mg/day); group 2: identical placebo; all: atenolol, antibiotics, anticonvulsants	**Harms:** Blood cells, blood pressure, EPS (SAS, AIMS), drowsiness, hepatic enzyme, NMS, seizure, tachycardia, weight	
Condition category: Schizophrenia and related	**Setting:** Inpatient	**N:** 11			
		Age, mean±SD (range): 13.7±1.6			
	Diagnostic criteria: DSM-III-TR, K-SADS, DICA-R	**Males %:** 54.6			
Funding: NR		**Caucasian %:** NR	**Prohibited drugs:** NR		
		Diagnostic breakdown			

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Risk of bias: High (subjective), High (objective)	**Inclusion criteria:** (1) schizophrenia with documented psychotic symptoms by 12 yr (DSM-III-TR), (2) intolerance, nonresponse, or both to ≥2 different neuroleptic drugs, (3) full-scale IQ ≥70 **Exclusion criteria:** (1) neurologic or medical disease	**(n):** disorganized (5), paranoid (1), undifferentiated (5) **Treatment naïve (n):** NR **Inpatients (n):** 11 **First episode psychosis (n):** 0 **GROUP 2** **N:** 10 **Age, mean±SD (range):** 14.4±2.9 **Males %:** 50 **Caucasian %:** NR **Diagnostic breakdown (n):** disorganized (5), undifferentiated (5) **Treatment naïve (n):** NR **Inpatients (n):** 10 **First episode psychosis (n):** 0	**GROUP 1** **Drug name:** Haloperidol **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 16±8 (7–27) **Concurrent treatments:** benzotropine **GROUP 2** **Drug name:** Clozapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 176±149 (25–525) **Concurrent treatments:** amoxicillin (1), penicillin (1)		
Luby et al., 2006 [48] **Country:** USA **Condition category:** ASD **Funding:** Industry **Risk of bias:** Medium (subjective), Low (objective)	**Recruitment dates:** Nov 1999 to Nov 2002 **Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) 2.5–6 yr, (2) autism or PDD-NOS (DSM-IV), (3) absence of other known significant CNS disorders, (4) absence of significant medical problems or other psychiatric disorders	**Enrolled:** 24 **Analyzed:** 23 **Completed:** NR **GROUP 1** **N:** 12 **Age, mean±SD (range):** 4.1±0.9 **Males %:** 75 **Caucasian %:** 91 **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 2** **N:** 12 **Age, mean±SD (range):** 4±1.1 **Males %:** 66.7 **Caucasian %:** 92	**Treatment duration:** 6 mo **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.1±0.3 (0.5–1.5) **Concurrent treatments:** applied behavior analysis (mean 21.2 hr/wk) **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR	**Benefits:** CARS **Harms:** Constipation, EPS, mortality, prolactin, SAE, sedation, WAE, weight change	Risperidone was well tolerated in preschoolers, but only minimal improvement in target symptoms was evident.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	requiring pharmacotherapy **Exclusion criteria:** NR	**Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR	**Daily dose (mg/day), mean±SD (range):** 1.4±0.6 (0.5–1.5) **Concurrent treatments:** applied behavior analysis (mean 11.3 hr/wk)		
Malone et al., 2001[49] **Country:** USA **Condition category:** ASD **Funding:** Industry **Risk of bias:** High (subjective), Medium (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) primary dx of PDD, (2) 5–17 yr, (3) at least moderate impairment on ≥2 of the first 28 items on the CPRS **Exclusion criteria:** (1) major medical problems, (2) seizure disorder or gross neurological deficit, (3) treatment with concomitant psychotropic medication, (4) history of previous treatment with haloperidol or olanzapine	**Enrolled:** 12 **Analyzed:** 12 **Completed:** 12 **GROUP 1** **N:** 6 **Age, mean±SD (range):** 7.3±1.9 (5–10.1) **Males %:** 66.7 **Caucasian %:** 66.7 **Diagnostic breakdown (n):** autistic disorder (5), PDD NOS (1) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (mild (1), moderate (2), severe (3)) **GROUP 2** **N:** 6 **Age, mean±SD (range):** 8.5±2.4 (4.9–11.8) **Males %:** 66.7 **Caucasian %:** 50 **Diagnostic breakdown (n):** autistic disorder (all) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (mild (0), moderate (3), severe (2))	**Treatment duration:** 6 wk **Run-in phase:** Yes **Run-in phase duration:** 1 wk **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Haloperidol **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.4±0.7 (0.5–2.5) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 7.9±2.5 (5–10) **Concurrent treatments:** NR	**Benefits:** CGI-S, CPRS, response (CGI-I) **Harms:** Dermatologic AE, EPS (AIMS, SAS), EPS, fatigue, tachycardia, weight changes	The use of olanzapine is promising in children with autistic disorder, although placebo-controlled and long-term studies are needed.
Mankoski et al.,	**Study design:**	**Enrolled:** NA	**GROUP 1**	**Benefits:** ABC-I,	Antipsychotic naïve

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
2013 [115] (see Marcus 2009 & Owen 2009) **Country:** USA **Condition category:** ASD **Funding:** Industry **Newcastle-Ottawa Scale:** 6/8 stars	Retrospective (pooled analysis), evaluate impact of prior antipsychotic exposure (PAE) on safety and tolerability outcomes in pediatric subjects receiving aripiprazole treatment	**Analyzed:** 313 **Completed:** NA **GROUP 1** **N:** 176 **Age, mean±SD (range):** see below **Males %:** see below **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** 176 **Inpatients (n):** NR **First episode psychosis (n):** NA **Comorbidities:** NR **GROUP 2** **N:** 80 **Age, mean±SD (range):** see below **Males %:** see below **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** 80 **Inpatients (n):** NR **First episode psychosis (n):** NA **Comorbidities:** NR **GROUP 3** **N:** 36 **Age, mean±SD (range):** see below **Males %:** see below **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis**	**Drug name:** Aripiprazole (antipsychotic naïve) **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo (antipsychotic naïve) **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 3** **Drug name:** Aripiprazole (PAE) **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 4** **Drug name:** Placebo (PAE) **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	CGI-S **Harms:** NA	subjects receiving aripiprazole for the treatment of irritability associated with ASD showed greater risk for weight gain and somnolence-related AEs than subjects receiving placebo. Changes in metabolic parameters in antipsychotic naïve subjects receiving aripiprazole treatment were small and similar to those in subjects receiving placebo.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		(n): NA **Comorbidities:** NR **GROUP 4** **N:** 21 **Age, mean±SD (range):** see below **Males %:** see below **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NA **Comorbidities:** NR **Overall Age, mean±SD (range):** mean(9.4-10) yr **Overall Males %:** 87.3-96.5%			
Marcus et al., 2009 [50] **Country:** USA **Condition category:** ASD **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** June 2006 to Jun 2008 **Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV-TR, ADI-R, CGI-S, ABC-I **Inclusion criteria:** (1) 6–17 yr, (2) DSM-IV-TR criteria for autistic disorder and behaviors such as tantrums, aggression, self–injury, or a combination, with a dx corroborated by	**Enrolled:** 218 **Analyzed:** 213 **Completed:** 178 **GROUP 1** **N:** 53 **Age, mean±SD (range):** 9.0±2.8 **Males %:** 88.7 **Caucasian %:** 69.8 **Treatment naïve (n):** 43 **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 2** **N:** 59 **Age, mean±SD (range):** 10±3.2 **Males %:** 84.7 **Caucasian %:** 69.5	**Treatment duration:** 8 wk **Run-in phase:** Yes **Run-in phase duration:** ≤6 wk **Permitted drugs:** anxiolytics, benztropine or propranolol, diphenhydramine (≤50 mg/day), psychotropic medication, sleep aids **Prohibited drugs:** antidepressants, antipsychotics, anxiolytics, mood stabilizers, neuroleptics, psychostimulants (washout ≥4 day) **GROUP 1** **Drug name:** Aripiprazole (low) **Dosing variability:** fixed **Target dose (mg/day):** 5 **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** analgesics	**Benefits:** ABC, CYBOCS, CGI-I, CGI-S, PedsQL, CGSQ, medication adherence, response (ABC-I, CGI-I), suicide **Harms:** Akathisia, BMI, dermatologic AE, ECG changes, EPS, EPS (AIMS, BAS, SAS), fatigue, glucose, lipid profile, mortality, prolactin, SAE, sedation, seizure/convulsion, somnolence, total AE, WAE, weight change, constipation	Aripiprazole was efficacious, safe, and well tolerated in children and adolescents with irritability assocated with autistic disorder.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	ADI-R certified trainer, (3) CGI-S score ≥4 and ABC Irritability subscale score ≥18 at screening and baseline, (4) ≥15 kg, (5) stable nonpharmacologic therapy **Exclusion criteria:** (1) bipolar disorder, psychosis, schizophrenia, major depression, fragile X syndrome, or another ASD, (2) history of NMS, (3) significant risk of committing suicide, (4) seizure in the past yr, (5) history of severe head trauma or stroke, (6) history or current evidence of any unstable medical condition or or an abnormal laboratory test result considered clinically significant, (7) antipsychotic treatment resistant, (8) known allergy or hypersensitivity to aripiprazole	**Treatment naïve (n):** 45 **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 3** **N:** 54 **Age, mean±SD (range):** 9.5±3.1 **Males %:** 92.6 **Caucasian %:** 77.8 **Treatment naïve (n):** 44 **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 4** **N:** 52 **Age, mean±SD (range):** 10.2±3.1 **Males %:** 92.3 **Caucasian %:** 67.3 **Treatment naïve (n):** 40 **Inpatients (n):** NR **First episode psychosis (n):** NR	and antipyretics (12), anxiolytics (2), benztropine (2), hypnotics and sedatives (2), propranolol (2) **GROUP 2** **Drug name:** Aripiprazole (medium) **Dosing variability:** fixed **Target dose (mg/day):** 10 **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** analgesics and antipyretics (12), anxiolytics (1), benztropine (1), hypnotics and sedatives (1) **GROUP 3** **Drug name:** Aripiprazole (high) **Dosing variability:** fixed **Target dose (mg/day):** 15 **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** analgesics and antipyretics (12), anxiolytics (1), benzotropine (5), hypnotics and sedatives (1) **GROUP 4** **Drug name:** Placebo **Dosing variability:** fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** analgesics and antipyretics (9), anxiolytics (3), hypnotics and sedatives (2), propranolol (1)		

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Martin et al., 2000 [116] **Country:** USA **Condition category:** Mixed conditions **Funding:** Non--industry **Newcastle-Ottawa Scale:** 6/8 stars	**Recruitment dates:** 1998 **Study design:** Retrospective **Setting:** Inpatient **Diagnostic criteria:** NR **Inclusion criteria:** All children and adolescents admitted to Riverview Hospital in 1998, (2) started on risperidone during their hospital stay, (3) no previous neuroleptic exposure, (4) no change in other psychotropic drugs used for 4 wk prior to risperidone introduction, (5) maintained on risperidone for ≥6 consecutive mo **Exclusion criteria:** NR	**Enrolled:** NA **Analyzed:** 70 **Completed:** 70 **GROUP 1** **N:** 37 **Age, mean±SD (range):** 12.5±2.4 yr **Males %:** 76 **Caucasian %:** 64 **Diagnostic breakdown (n):** Psychotic (9), affective (11), anxiety (12), disruptive (30), PDD/MR (10), polysubstance (0), ED (0) **Treatment naïve (n):** NR **Inpatients (n):** 37 **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 33 **Age, mean±SD (range):** 13.5±2.9 yr **Males %:** 49 **Caucasian %:** 61 **Diagnostic breakdown (n):** Psychotic (2), affective (19), anxiety (11), disruptive (27), PDD/MR (8), polysubstance (2), ED (2) **Treatment naïve (n):** NR **Inpatients (n):** 33 **First episode psychosis (n):** NR **Comorbidities:** NR	**Treatment duration:** ≥6 mo **Run-in phase:** Yes **Run-in phase duration:** 4 wk **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 2.8±1.9 **Concurrent treatments:** Valproate (12), SSRI (8), stimulant (8), α_2 agonist (8), traditional neuroleptic (0) **GROUP 2** **Drug name:** Control **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** Valproate (10), SSRI (9), stimulant (6), α_2 agonist (6), traditional neuroleptic (9)	**Benefits:** NR **Harms:** Weight (BMI, BMI z-score)	Studies of children and adolescents are needed to prospectively monitor weight change (as well as serum glucose, liver enzyme, and triglyceride levels) during chronic exposure to risperidone and other atypical neuroleptics. Long-term effects, as well as changes following drug discontinuation are likewise needed. Until those empirical data become available, it seems prudent to recommend careful monitoring of height, weight, and BMI of all children treated with atypical antipsychotics, as well as to consider glucose, liver enzyme, and lipid levels as part of their routine safety monitoring.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Masi et al., 2015 [52] **Country:** Italy **Condition category:** Bipolar II (hypomanic) **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** Jan 2013 to Jan 2014 **Study design:** RCT (parallel) **Setting:** Inpatient/outpatient **Diagnostic criteria:** DSM-IV-TR, K-SADS-PL **Inclusion criteria:** (1) diagnosis of Bipolar II hypomanic episode as confirmed by DSM-IV-TR, K-SADS-PL and YMRS total score of ≥17 at baseline, (2) CGI-S≥4, (3) CGAS≤50 **Exclusion criteria:** NR	**Enrolled:** 24 **Analyzed:** 22 **Completed:** 22 **GROUP 1** **N:** 12 **Age, mean±SD (range):** 14.9±1.1 **Males %:** 41.7 **Caucasian %:** 100 **Diagnostic breakdown (n):** hypomanic (all) **Treatment naïve (n):** 12 **Inpatients (n):** 3 **First episode psychosis (n):** NR **Comorbidities:** CD (all) ADHD (2), anxiety disorders (3), substance use disorder (1), eating disorder NOS (1) **GROUP 2** **N:** 10 **Age, mean±SD (range):** 15.1±1.8 **Males %:** 70 **Caucasian %:** 100 **Diagnostic breakdown (n):** hypomanic (all) **Treatment naïve (n):** 12 **Inpatients (n):** 3 **First episode psychosis (n):** NR **Comorbidities:** CD (all), ADHD (3), anxiety disorders (2), substance use disorder (2), eating disorder NOS (1)	**Treatment duration:** 12 wk **Run–in phase:** NR **Run–in phase duration:** NR (all treatment naïve) **Permitted drugs:** Methyphenidate at stable dose in 1 patient in risperidone group **Prohibited drugs:** Psychotropics≤6mo **GROUP 1** **Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 163.30±55.20 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.90±0.60 **Concurrent treatments:** NR	**Benefits:** YMRS, CGI-S, CGAS, HDRS, HAM-A, MOAS, response **Harms:** BMI, prolactin, somnolence, fatigue, EPS, ECG	Risperidone and quetiapine did not differ in BMI increase according to the main analysis, although the post hoc analysis suggests a possible BMI increase with risperidone but not with quetiapine. Data on higher prolactin increase during risperidone treatment, compared with quetiapine, are in line with previous studies. However, our findings about safety, namely, the modest BMI increase and the absence ofQTc prolongation, should be cautiously considered in the context of the limited time of the study.
Masi et al., 2013 [51] **Country:** Italy	**Recruitment Dates:** NR	**Enrolled:** 69 **Analyzed:** 69 **Completed:** 69	**Treatment duration:** ≥ 12 wk **Run-in phase:** NR **Run-in phase duration:** NR	**Benefits:** C-GAS, CGI-S, CGI-I, response	In tic-related pediatric OCD, augmentation of

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Condition category: OCD **Funding:** No funding provided **Risk of Bias:** High (subjective), Medium (objective)	**Study design:** NRCT (parallel) **Diagnostic criteria:** DSM-IV, K-SADS-PL (OCD), DSM-IV-TR (Tic) **Setting:** Outpatient **Inclusion criteria:** Diagnosis of OCD, CGI score ≥ 4 and C-GAS score ≤ 60. Comorbid tic disorder, ≥ 40 on YGTSS, non-responder to SSRI **Exclusion criteria:** Diagnosis of mental retardation, PDD, schizophrenia	**GROUP 1:** **N:** 35 **Age, mean±SD (range):** 13.3±2.2 yr **Males %:** 94.3% **Caucasian %:** NR **Diagnostic breakdown (n):** OCD with comorbid tic disorder (35) **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** GAD (7), separation AD (4), panic disorder (2), social phobia (13), simple phobia (4), depression (8), BP (6), ADHD (6), ODD (9) **GROUP 2:** **N:** 34 **Age, mean±SD (range):** 13.9±2.5 yr **Males %:** 85.3% **Caucasian %:** NR **Diagnostic breakdown (n):** OCD with comorbid tic disorder (34) **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** GAD (1), separation AD (1), panic disorder (1), social phobia (6), depression (4), BP (2), ADHD (14), ODD (7)	**Permitted drugs:** SSRI **Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone **Dosing variability:** Variable **Target dose (mg/day):** 3 mg/day **Daily dose (mg/day), mean±SD (range):** 1.7±0.8 (0.5-3) mg/day **Concurrent treatments:** SSRI (35), mood stabilizers (3), stimulants (1), psychotherapy (20) **GROUP 2:** **Drug name:** Aripiprazole **Dosing variability:** Variable **Target dose (mg/day):** 12.5 mg/day **Daily dose (mg/day), mean±SD (range):** 8.9±3.1 (2.5-12.5) mg/day **Concurrent treatments:** SSRI (34), mood stabilizers (1), stimulants (1), psychotherapy (14)	**Harms:** Weight, sedation, tremors	SSRIs with risperidone or aripiprazole was tolerated and effective in about half of the patients who did not respond to SSRIs alone.
McCracken et al., 2002 [53]	**Recruitment dates:** Jun 1999 to Apr 2001	**Enrolled:** 101 **Analyzed:** 101	**Treatment duration:** 8 wk **Run-in phase:** Yes	**Benefits:** ABC, CYBOCS, CGI-I,	Risperidone was effective and well

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Completed: 80	**Run-in phase duration:** 1–4 wk	CGI-S, RFRLRS, VAS, AIMS, Cognitive, medication adherence, patient, parent/care provider reported outcomes (diet/intake, sleep), response **Harms:** Behavioral issues, blood cells, BMI, constipation, dyskinesia, dermatologic AE, ECG changes, EPS (AIMS, SAS), fatigue, liver function, prolactin, prolactin-related AE, SAE, seizure, tachycardia, WAE, weight change	tolerated for the treatment of tantrums, aggression, or self-injurious behavior in children with autistic disorder. Discontinuation, after 6 month of treatment, was associated with rapid return of disruptive and aggressive behavior in most subjects.
Country: USA **Condition category:** ASD **Funding:** Industry, Government, Foundation **Risk of bias:** Medium (subjective), Medium (objective)	**Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV, ADI-R **Inclusion criteria:** (1) ASD (DSM-IV), (2) 5–17 yr, (3) weight ≥15 kg, (4) score ≥18 on the Irritability subscale of the ABC at baseline, (5) free of serious medical disorders and of other psychiatric disorders requiring medication, (6) medication free for at least 2 wk for all psychotropic medications (4 wk for fluoxetine or depot neuroleptics), (7) anticonvulsants used for the treatment of a seizure disorder were permitted if the dosage had been stable for 4 wk and the patient had been seizure free for ≥6 mo, (8) CGI-S score ≥ 4 at baseline, (9) mental age ≥18 mo as measured by the age-appropriate form of the IQ test, (10) inpatients or outpatients	**GROUP 1** **N:** 49 **Age, mean±SD (range):** NR **Males %:** 80 **Caucasian %:** NR **Treatment naïve (n):** 45 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (average/above average IQ (3), borderline IQ (8), mild/ moderate retardation (20), severe retardation (15)) **GROUP 2** **N:** 52 **Age, mean±SD (range):** NR **Males %:** 83 **Caucasian %:** NR **Treatment naïve (n):** 51 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (average/above average IQ (2), borderline IQ (4), mild/ moderate retardation (23), severe retardation (16))	**Permitted drugs:** anticonvulsants (constant dose ≥4 wk and seizure-free for ≥6 mo), benztropine **Prohibited drugs:** antihistamines, ceterazine, erythromycin, metoclopromide, pseudoephedrine, and any drug that may impact risperidone concentrations or lead to drug interactions; psychotropics **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.8±0.7 (0.5–3.5) **Concurrent treatments:** anticonvulsants (2) **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 2.4±0.6 (0.5–3.5) **Concurrent treatments:** anticonvulsants (2)		

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	Exclusion criteria: (1) receiving a psychotropic drug that was deemed effective for the treatment of aggression, tantrums, or self-injurious behavior, (2) positive β-HCG pregnancy test, (3) evidence of a prior adequate trial with risperidone, (4) evidence of hypersensitivity to risperidone, (5) past history of NMS, (6) DSM-IV dx of schizophrenia, another psychotic disorder, or substance abuse, (7) significant medical condition, (8) weight <15 kg				
McGorry et al., 2013 [54] **Country:** Australia **Condition category:** Schizophrenia and related **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** August 2000 to May 2006 **Study design:** RCT (parallel) **Setting:** Outpatient **Diagnostic criteria:** Ultra-high risk: (1) the presence of attenuated (subthreshold) psychotic symptoms within the previous 12 months; (2) a history of brief self-limited psychotic symptoms, which spontaneously	**Enrolled:** 87 **Analyzed:** NR **Completed:** 56 **GROUP 1** **N:** 43 **Age, mean±SD (range):** 17.6±3.0 **Males %:** 35 **Caucasian %:** NR **Treatment naïve (n):** 100 **Inpatients (n):** 0 **First episode psychosis (n):** UHR **GROUP 2** **N:** 44 **Age, mean±SD (range):** 18.0±2.7	**Treatment duration:** 52 wk **Run-in phase:** NA **Run-in phase duration:** NA **Permitted drugs:** NR **Prohibited drugs:** mood-stabilizing medications **GROUP 1** **Drug name:** Cognitive therapy + risperidone **Dosing variability:** variable **Target dose (mg/day):** up to 2mg/day **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	**Benefits:** BPRS, SANS, GAF, HDRS, quality of life, transition rates **Harms:** UKU	The equivalent transition rates fail to provide support for the first-line use of antipsychotic medications in patients at ultra-high risk of psychosis, and an initial approach with supportive therapy is likely to be effective and carries fewer risks.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	resolve, within the previous 12 months; and (3) a presumed genetic vulnerability to psychotic disorder plus persistent low functioning for at least 1 month within the previous 12 months **Inclusion criteria:** 14-30 yrs; see above criteria **Exclusion criteria:** (1) known history of a previous psychotic or manic episode, (2) history of a medical condition that may account for symptoms leading to initial referral (eg, epilepsy), (3) clinically relevant neurologic, biochemical, or hematologic abnormalities, (4) serious coexisting illnesses, (5) lifetime antipsychotic dose of 15mg of haloperidol (or equivalent) or greater, (6) any previous or current use of mood-stabilizing medication, (7) history of severe drug allergy, (8) intellectual disability (IQ < 70), (9) pregnancy or lactation,	**Males %:** 39 **Caucasian %:** NR **Treatment naïve (n):** 100 **Inpatients (n): 0** **First episode psychosis (n):** UHR	**GROUP 2** **Drug name:** Cogntive therapy + placebo **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 0 **Concurrent treatments:** NR		

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	(10) insufficient English language				
Migliardi et al., 2009 [117] **Country:** Italy **Condition category:** Mixed conditiopns **Funding:** NR **Risk of bias:** 7/8 stars	**Recruitment dates:** NR **Study design:** Retrospective cohort **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) children and adolescents seen at the Division of Child and Neurology at the University of Messina, Italy, (2) not previously treated with antipsychotics for various psychiatric disorders, (3) completed at least 12 months of treatment on only one antipsychotic and no co-medication **Exclusion criteria:** NR	**Enrolled:** 42 **Analyzed:** 41 **Completed:** 42 **GROUP 1** **N:** 13 **Age, mean±SD (range):** 14.1 **Males %:** 53.8 **Caucasian %:** NR **Treatment naïve (n):** all **Diagnostic breakdown (n):** DBD (4), early-onset schizophrenia (3), BD (2), autism/PDD (2), OCD (1) **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 29 **Age, mean±SD (range):** 10.7 **Males %:** 78.6 **Caucasian %:** NR **Treatment naïve (n):** all **Diagnostic breakdown (n):** Autism/PDD (13), DBD (9), early-onset schizophrenia (2), OCD (2), Tic disorder (2) **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** NR	**Treatment duration:** 12 mo **Run–in phase:** No **Run–in phase duration:** NA **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 8.1 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.8 **Concurrent treatments:** NR	**Benefits:** NA **Harms:** prolactin-related AE, prolactin	After adjusting for dose and greater potency of risperidone, the increase in prolactin levels during risperidone treatment was 10.3 times higher than during olanzapine treatment.
Miral et al., 2008 [55] **Country:** Turkey **Condition**	**Recruitment dates:** NR **Study design:** RCT (parallel)	**Enrolled:** 30 **Analyzed:** 28 **Completed:** 28 **GROUP 1**	**Treatment duration:** 24 wk **Run-in phase:** Yes **Run-in phase duration:** 1–2 wk **Permitted drugs:** antianalgesics,	**Benefits:** ABC, CGI, RFRLRS **Harms:** Blood pressure,	Risperidone was more effective than haloperidol, showing improvements in behavioral

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
category: ASD **Funding:** Industry **Risk of bias:** Medium (subjective), Medium (objective)	**Setting:** NR **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) 8–18 yr, (2) parental informed consent, (3) agree to followup **Exclusion criteria:** (1) epilepsy, (2) concomitant neuropsychiatric illness, (3) psychotic disorder or symptoms, (4) other PDDs	**N:** 15 **Age, mean±SD (range):** 10.9±2.9 (7–17) **Males %:** 86.7 **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (0), psychosis (0) **GROUP 2** **N:** 15 **Age, mean±SD (range):** 10±2.7 (7–17) **Males %:** 73.3 **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (0), psychosis (0)	antibiotics, anticholinergics, antipyretics, decongestants **Prohibited drugs:** benzodiazepines/other sedatives **GROUP 1** **Drug name:** Haloperidol **Dosing variability:** variable **Target dose (mg/day):** 0.08 mg/kg/day **Daily dose (mg/day), mean±SD (range):** 2.6±1.3 (1–5.7) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** 0.08 mg/kg/day **Daily dose (mg/day), mean±SD (range):** 2.6±0.8 (1.2–4.0) **Concurrent treatments:** NR	constipation, EPS (ESRS, UKU), height, parkinsonism/ dystonia/ dyskinesia (ESRS), prolactin-related AE, SAE, weight	symptoms and social skills.
Mozes et al., 2006 [56] **Country:** Israel **Condition category:** Schizophrenia and related **Funding:** No funding **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Inpatient **Diagnostic criteria:** DSM-IV, K-SADS **Inclusion criteria:** (1) hospitalized childhood-onset schizophrenic children **Exclusion criteria:** (1) MR	**Enrolled:** 25 **Analyzed:** 25 **Completed:** 20 **GROUP 1** **N:** 12 **Age, mean±SD (range):** 11.5±1.6 (8.5–14) **Males %:** 41.7 **Caucasian %:** NR **Diagnostic breakdown (n):** disorganized schizophrenia (3), paranoid schizophrenia (2), schizophreniform disorder (6), unspecified schizoprehenia (1) **Treatment naïve (n):** NR	**Treatment duration:** 2.8 mo **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** biperiden, prior nonantipsychotics (continued for 2–12 wk) **Prohibited drugs:** NR **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 8.2±4.4 (2.5–20) **Concurrent treatments:** biperiden (2), carbamazepine (2), citalopram	**Benefits:** BPRS, CGAS, PANSS, response **Harms:** BAS, SAS akathisia, prolactin, WAE, weight change	Risperidone and olanzapine were efficacious and well tolerated in pediatric inpatients with child-onset schizophrenia.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Inpatients (n): all **First episode psychosis (n):** NR **Comorbidities:** ADHD (2), familial mediterranean fever (1), MR (0), tic disorder (1) **GROUP 2** **N:** 13 **Age, mean±SD (range):** 10.7±1.4 (8.8–13.3) **Males %:** 38.5 **Caucasian %:** NR **Diagnostic breakdown (n):** disorganized schizophrenia (4), paranoid schizophrenia (4), schizophreniform disorder (4), unspecified schizoprehenia (1) **Treatment naïve (n):** NR **Inpatients (n):** all **First episode psychosis (n):** NR **Comorbidities:** ADHD (1), epilepsy (2), MR (0), neurofibromatosis (1), OCD (3)	(1), colchicine (1), methylphenidate (2), promethizine (2), valproic acid (1) **GROUP 2** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.6±1 (0.3–4.5) **Concurrent treatments:** biperiden (4), citalopram (2), fluoxetine (1), phenytoin (1), promethizine (1), valproic acid (1)		
Nagaraj et al., 2006 [57] **Country:** India **Condition category:** ASD **Funding:** Industry, Academic **Risk of bias:** Low (subjective), Low	**Recruitment dates:** Jan 2002 to Dec 2003 **Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1)	**Enrolled:** 40 **Analyzed:** 39 **Completed:** 39 **GROUP 1** **N:** 19 **Age, mean±SD (range):** 4.8±1.7 **Males %:** 84.2 **Caucasian %:** NR **Treatment naïve (n):** 15 **Inpatients (n):** 0 **First episode psychosis**	**Treatment duration:** 6 mo **Run-in phase:** Yes **Run-in phase duration:** ≥1 mo **Permitted drugs:** antiepileptics **Prohibited drugs:** no other drugs permitted **GROUP 1** **Drug name:** Risperidone **Dosing variability:** fixed **Target dose (mg/day):** NR	**Benefits:** CARS, CGAS, response (CARS, CGAS, Global Impression of Parents) **Harms:** Dyskinesia, sedation, weight change	Risperidone improved global functioning and social responsiveness, reduced hyperactivity and aggression, and was well tolerated in children with autism.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
(objective)	≤12 yr, (2) autism (DSM-IV) **Exclusion criteria:** (1) severe MR, (2) any significant coexisting disease or illness, (3) severe malnutrition	**(n):** NR **Comorbidities:** aggression (9), irritability (17), seizures (5), self-injurious behavior (7) **GROUP 2** **N:** 21 **Age, mean±SD (range):** 5.3±1.7 **Males %:** 90 **Caucasian %:** NR **Treatment naïve (n):** 16 **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** aggression (11), irritability (19), seizures (3), self-injurious behavior (5)	**Daily dose (mg/day), mean±SD (range):** 1 (0.5–1) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo **Dosing variability:** fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1 (0.5–1) **Concurrent treatments:** NR		
NCT00194012, 2013 [58] **Country:** USA **Condition category:** Bipolar **Funding:** Industry, Institution (hospital) **Risk of bias:** High (subjective). High (objective)	**Recruitment dates:** August 2004-May 2012 **Study design:** RCT **Setting:** Outpatient **Diagnostic criteria:** (1) DSM-IV criteria for either cyclothymia, or BP NOS based on K-SADS-PL and WASH-U K-SADS, (2) a clinical interview with a child and adolescent psychiatrist **Inclusion criteria:** (1) outpatient, (2) 5-17	**Enrolled:** 59 **Analyzed:** NR **Completed:** 21 (15 Group 1; 6 Group 2) **GROUP 1** **N:** 30 **Age, mean±SD (range):** <18 yr (all) **Males %:** 66.7 **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** None **First episode psychosis (n):** NR **GROUP 2** **N:** 29 **Age, mean±SD (range):** <18 yr (all) **Males %:** 51.7 **Caucasian %:** NR	**Treatment duration:** 12 wk, plus 6 wk open label extension **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** psychotropic agents taken <1 wk of baseline (2 wk for fluoxetine; 3 days for psychostimulants) **GROUP 1** **Drug name:** Abilify (aripiprazole) **Dosing variability:** 2-15 mg **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo	**Benefits:** YMRS **Harms:** AEs (major and minor)	NR

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	yr, (3) symptoms of mania, depression, or both <2 wk, (4) offspring of a parent with BP spectrum disorder, (5) another 1st or 2nd degree relative with a mood disorder, (6) participated in ≥4 sessions of psychotherapy and continues to have clinically significant symptomatology **Exclusion criteria:** (1) intolerance to APZ at doses of 0.1mg/kg/day, (2) manic episode with APZ monotherapy at a dose of 0.2 mg/kg/day, (3) contraindications for which tx with APZ, (4) ASD, Asperger's disorder, Rett's syndrome or other PDD, (5) mental retardation, (6) allergic or hypersensitive to APZ, (7) unable to swallow pills/capsules, (8) hospitalization	**Treatment naïve (n):** NR **Inpatients (n):** None **First episode psychosis (n):** None	**Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR		

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	during the study, (9) started a new psychotherapeutic intervention <4 wk prior to randomization, (10) general medical or neurological condition that: i) may be the etiology of the pts mood disorder, ii) contraindicate tx with an AAP, iii) may interfere with the interpretation of clinical response to APZ; (11) other psychotropic agents <1 wk of baseline (2 wk for fluoxetine; 3 days for psychostimulants); (12) <6 mo prior to randomization: i) a suicide attempt requiring medical/ psychiatric, ii) met DSM-IV criteria for SA, (13) pt who are pregnant or lactating, (14) sexually active				

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	females, not using an adequate birth control				
NCT00619190, 2013 [118] **Country:** USA **Condition category:** ASD **Funding:** Institution (University) **Newcastle-Ottawa Scale:** 4/8	**Recruitment dates:** NR **Study design:** Controlled before-after study **Setting:** NR **Diagnostic criteria:** NR **Inclusion criteria:** NR **Exclusion criteria:** NR	**Enrolled:** 30 **Analyzed:** **Completed:** 29 **GROUP 1** **N:** 21 **Age, mean±SD (range):** 8.3±3.75 **Males %:** 90.5 **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 2** **N:** 9 **Age, mean±SD (range):** 11.1±4.5 **Males %:** 88.9 **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR	**Treatment duration:** 12 wk **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Apriprazole **Dosing variability:** 1-30 mg **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 2** **Drug name:** No medication **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	**Benefits:** ABC-I, CGI-S, ABC-Lethargy/Social Withdrawal **Harms:** AEs (major and minor)	
NCT01149655, 2014 [59] **Country:** Multiple countries **Condition category:** Schizophrenia and related **Funding:** Industry	**Recruitment dates:** July 2011-Dec 2013 **Study design:** RCT **Setting:** Outpatient **Diagnostic criteria:** DSM-IV-TR diagnosis of schizophrenia	**Enrolled:** 146 **Analyzed:** **Completed:** 21 (15 (group 1), 6 (groupd 2)) **GROUP 1** **N:** 98 **Age, mean±SD (range):** 15.3±1.3 (male); 15.4±1.1 (female) **Males %:** 63.3 **Caucasian %:** NR	**Treatment duration:** 52 wk **Run-in phase:** Yes (stabilized on 10-30 mg/day of aripiprazole prior to randomization) **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Apriprazole	**Benefits:** Relapse Rate (CGI-I/S, PANSS, hospitalization, suicide ideation, violent/aggressive behavior), % exacerbation or relapse/impending relapse, % responders, % achieved remission,	

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
(pharmaceutical) **Risk of bias:** High (subjective). High (objective)	**Inclusion Criteria:** (1) schizophrenia, (2) hx of illness ≥6 mo prior to screening, (3) shown previous response to antipsychotic tx (other than clozapine), (4) currently being treated with oral or depot antipsychotics other than clozapine, (5) hx of relapse and/or exacerbation of symptoms when off antipsychotic tx. **Exclusion criteria:** (1) dx other than schizophrenia, (2) delirium, dementia, amnesia or other cognitive disorders, (3) psychotic symptoms better accounted for by another medical condition(s) or direct effect of a substance, (4) comorbid dx of ADD or ADHD, (5) tx with stimulants at any time over the last 1 yr prior to screening, (6) any neurodevelopmental disorder, except Tourette's syndrome, (7) acute depressive symptoms ≤30 days prior to screening, (8) DSM-IV-TR criteria for substance dependence	**Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 2** **N:** 48 **Age, mean±SD (range):** 15.6±1.1 (males), 15.3±1.0 (females) **Males %:** 70.8 **Caucasian %:** NR **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NR	**Dosing variability:** 10-30 mg/day **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	% discontinued, CGAS **Harms:** AEs (minor and serious)	

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	≤180 days prior to screening, (9) Hx of: epilepsy, seizures, severe head trauma, stroke, or other unstable medical conditions, subclinical hypothyroidism (TSH ≥ 4.0 mIU/L), known hypothyroidism or hyperthyroidism (unless stabilized with medication for ≥ 90 days prior to entry into Phase 1 or Phase 2), uncontrolled diabetes, labile or unstable diabetes (brittle diabetes), newly diagnosed diabetes, or clinically significant abnormal blood glucose levels				
Norris et al., 2011 [119] **Country:** Canada **Condition category:** Eating disorders (Anorexia nervosa) **Funding:** Non-industry **Newcastle-Ottawa Scale:** 7/8 stars	**Recruitment dates:** Jan 2000 to Dec 2006 **Study design:** Retrospective **Setting:** inpatient and outpatient **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) 10-17 yr, (2) female, (3) diagnosed with AN or EDNOS according to DSM-IV **Exclusion criteria:** (1)	**Enrolled:** 86 **Analyzed:** 86 **Completed:** 86 **GROUP 1** **N:** 43 **Age, mean±SD (range):** 14.4±1.9 yr **Males %:** 0 **Caucasian %:** NR **Diagnostic breakdown (n):** ANR (29), ANBP (2), EDNOS-R (12) **Treatment naïve (n):** NR **Inpatients (n):** 35 **First episode psychosis (n):** NR **Comorbidities:** Anxiety (29), depression (26),	**Treatment duration:** 2 wk for weight outcomes **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** SSRI/SNRI (17), benzodiazepine (3) (at the time of olanzapine initiation) **Prohibited drugs:** NR **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** flexible **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** [median (IQR)] 5.0 (3.75-7.5) **Concurrent treatments:**	**Benefits:** CDI, MASC, EDI-2DT, EDI-2BD **Harms:** change in body composition (weight, BMI), dyslipidemia, liver function test, sedation, rebound weight loss and increased psychological stress after initial discontinuation of olanzapine	Patients treated with olanzapine presented with greater acuity and more complex psychopathology than those patients not treated with olanzapine, which made comparisons regarding efficacy of the drug impossible. The observed side-effect profile noted in patients treated with olanzapine indicates the need for close monitoring during the entire

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	males, (2) concurrent diagnosis of psychosis, or a concurrent illness with psychotic features, or whose primary treatment was not under the direction of the eating disorder team	obsessive compulsive disorder (3) **GROUP 2** **N:** 43 **Age, mean±SD (range):** 14.8±1.6 yr **Males %:** 0 **Caucasian %:** NR **Diagnostic breakdown (n):** ANR (29), ANBP (2), EDNOS-R (12) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities: :** Anxiety (13), depression (15), obsessive compulsive disorder (1)	SSRI/SNRI (17), benzodiazepine (3) **GROUP 2** **Drug name:** Not olanzapine **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR		course of treatment, regardless of the patient's absolute weight.
Novaes et al., 2008 [120] **Country:** Brazil **Condition category:** ASD **Funding:** Foundation **Newcastle-Ottawa Scale:** 8/8 stars	**Recruitment dates:** Jan 2001 to June 2006 **Study design:** Retrospective cohort **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) ASD, (2) behavioral disturbances (psychomotor agression or agitation) **Exclusion criteria:** NR	**Enrolled:** NA **Analyzed:** 26 **Completed:** 26 **GROUP 1** **N:** 1 **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** Aggression/Agitation (26), MR (20) **GROUP 2** **N:** 13 and 5	**Treatment duration:** 17 mo (mean) **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Typical antipsychotic **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 2** **Drug name:** Risperidone/Risperidone + Typical antipsychotic	**Benefits:** Response (CGI-I) **Harms:** NR	SGAs appeared to reduce agitation and aggression in patients with ASD.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Age, mean±SD (range): NR **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** see group 1 **GROUP 3** **N:** 4 **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** see group 1 **GROUP 4** **N:** 3 **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** see group 1	**Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 3** **Drug name:** Atypical antipsychotic (not risperidone) **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 4** **Drug name:** Typical + atypical antipsychotic **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** one treatment (12), ≥2 treatments (7)		
O'Donoghue et al., 2014 [121] **Country:** Austria **Condition**	**Recruitment dates:** January 2001 to August 2005 **Study design:** Prospective cohort	**Enrolled:** 44 **Analyzed:** 36 **Completed:** 36 **GROUP 1** **N:** 16	**Treatment duration:** mean 31 wk **Run-in phase:** No **Run-in phase duration:** NA **Permitted drugs:** SSRI	**Benefits:** NR **Harms:** triglycerides, BMI, cholesterol	One-third of children and adolescents had abnormal serum triglycerides and cholesterol; however, a dose–

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
category: Schizophrenia and related **Funding:** NR **Newcastle-Ottawa Scale:** 3/8 stars	**Setting:** NR **Diagnostic criteria:** DSM-III **Inclusion criteria:** (1) 13-17 yr, (2) schizophrenia spectrum disorder, (3) no previous antipsychotic medications **Exclusion criteria:** (1) IQ <70	**Age, mean±SD (range):** 15.9±1.2 (all groups) **Males %:** 58 **Caucasian %:** NR **Treatment naïve (n):** 16 **Inpatients (n):** NR **First episode psychosis (n):** 16 **GROUP 2** **N:** 20 **Age, mean±SD (range):** 15.9±1.2 (all groups) **Males %:** 58 **Caucasian %:** NR **Treatment naïve (n):** 20 **Inpatients (n):** NR **First episode psychosis (n):** 20	**Prohibited drugs:** NR **GROUP 1** **Drug name:** Olanzapine & quetiapine **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** SSRI (31% all groups) **GROUP 2** **Drug name:** Risperidone **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** SSRI (31% all groups)		response was not demonstrated. Olanzapine and quetiapine had a greater increase in serum triglycerides.
Oh et al., 2013 (122) **Country:** South Korea **Condition category:** Bipolar I, II, NOS **Funding:** NR **Newcastle-Ottawa Scale:** 6/8 stars	**Recruitment dates:** Jan 2010 to Oct 2011 **Study design:** Retrospective **Setting:** Outpatient **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) Male and female outpatients, (2) aged 4 to 18 years, (3) DSM-IV diagnosis of bipolar I disorder, bipolar II disorder, bipolar disorder, and bipolar affective disorder	**Enrolled:** 183 **Analyzed:** 127 **Completed:** 32 **GROUP 1** **N:** 62 **Age, mean±SD (range):** 13.16±2.80 yr **Males %:** 66.1 **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** See below **GROUP 2** **N:** 65	**Treatment duration:** 7-8 mo **Run–in phase:** NR **Run–in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Aripiprazole **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 9.58±5.38 **Concurrent treatments:** See below **GROUP 2** **Drug name:** Others **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD	**Benefits:** ADHD RS-IV, CGI-S, CGI-I **Harms:** Akathisia, sedation, nausea	The early treatment effects and long-term tolerability of aripiprazole were found to be excellent compared with those of other atypical antipsychotics. The superior treatment effects of aripiprazole, which was also associated with comparatively mild side effects, may enhance the treatment compliance of pediatric patients and their guardians. However, these

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	Exclusion criteria: (1) Another diagnosis as main reason for treatment (eg: tic disorder, ADHD), (2) who visited the clinic only once or did not take medication	**Age, mean±SD (range):** 11.46±3.95 yr **Males %:** 76.9 **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** See below **Overall comorbidities:** ADHD (50), tic related disorders (17), conduct disorders and ODD (5), autism spectrum disorder (12)	**(range):** Risperidone (1.46±1.08), quetiapine (207.46±200.53), paliperidone (4.50±2.12) **Concurrent treatments:** See below **Overall concurrent treatments:** mood stabilizers (20), methyphenidate (34), atomoxetine (12), antidepressants (27)		results must be confirmed in the future through multi-center, double-blind, placebo-control studies.
Olfson et al., 2012 [123] **Country:** USA **Condition category:** Schizophrenia and related **Funding:** Government **Newcastle-Ottawa Scale:** 7/8 stars	**Recruitment dates:** Medicaid claims file 2001-2005 **Study design:** Retrospective cohort **Setting:** Inpatients (<10%) and outpatients **Diagnostic criteria:** ICD-9-CM **Inclusion criteria:** (1) 6-17 yr, (2) eligible for Medicaid (fee-for-service plans) for ≥180 days after antipsychotic Initiation, (3)	**Enrolled:** 1745 **Analyzed:** 1745 **Completed:** NA **GROUP 1** **N:** 805 **Age, mean±SD (range):** NR **Males %:** 62 **Caucasian %: 38** **Treatment naïve (n):** 805 **Inpatients (n):** **First episode psychosis (n):** NR **GROUP 2** **N:** 382 **Age, mean±SD (range):** NR **Males %:** 69 **Caucasian %:** 38	**Treatment duration:** **Run-in phase:** **Run-in phase duration:** **Permitted drugs:** None **Prohibited drugs:** None **GROUP 1** **Drug name:** Risperidone **Dosing variability:** **Target dose (mg/day):** **Daily dose (mg/day), mean±SD (range):** **Concurrent treatments:** **GROUP 2** **Drug name:** Olanzapine **Dosing variability:** **Target dose (mg/day):** **Daily dose (mg/day), mean±SD**	**Benefits:** Medication adherence (all-cause discontinuation), psychiatric hospital admission **Harms:** NR	The results suggest that rapid antipsychotic medication discontinuation and psychiatric hospital admission are common in the community treatment of early-onset schizophrenia.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	schizophrenia and related disorders **Exclusion criteria:** (1) not enrolled in Medicare, (2) free of any antipsychotic prescriptions for at least 180 continuous days before filling a risperidone, olanzapine, aripiprazole, quetiapine, or ziprasidone prescription of ≤30 days supply	**Treatment naïve (n):** 382 **Inpatients (n):** **First episode psychosis (n):** NR **GROUP 3** **N:** 260 **Age, mean±SD (range):** NR **Males %:** 52 **Caucasian %: 48** **Treatment naïve (n):** 260 **Inpatients (n):** **First episode psychosis (n):** NR **GROUP 4** **N:** 173 **Age, mean±SD (range):** NR **Males %:** 55 **Caucasian %: 42** **Treatment naïve (n):** 173 **Inpatients (n):** **First episode psychosis (n):** NR **GROUP 5** **N:** 125 **Age, mean±SD (range):** NR **Males %:** 57 **Caucasian %:** 44 **Treatment naïve (n):** 125 **Inpatients (n):** **First episode psychosis (n):** NR	**(range):** **Concurrent treatments:** **GROUP 3** **Drug name:** Quetiapine **Dosing variability:** **Target dose (mg/day):** **Daily dose (mg/day), mean±SD (range): Concurrent treatments:** **GROUP 4** **Drug name:** Aripiprazole **Dosing variability:** **Target dose (mg/day):** **Daily dose (mg/day), mean±SD (range): Concurrent treatments:** **GROUP 5** **Drug name:** Ziprasidone **Dosing variability:** **Target dose (mg/day): Daily dose (mg/day), mean±SD (range):** **Concurrent treatments:**		
Omranifard et al, 2013 [60] **Country:** Iran	**Recruitment dates:** 2009 **Study design:** RCT	**Enrolled:** 90 **Analyzed:** 87 **Completed:** 87 **GROUP 1**	**GROUP 1** **Drug name:** risperidone **Dosing variability:** 0.25-1 mg/d **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD**	**Benefits:** Efficacy (frequency of masturbation) **Harms:** None	In contrast to the behavioral treatment which was only effective in younger ages in the control

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Condition category: Behavioral issues **Funding:** Institution (University) **Risk of bias:** High (subjective), NA (objective)	**Setting:** Outpatient **Diagnostic criteria:** NR **Inclusion criteria:** (1) informed consent; (2) boys and girls 3-7 yr; (3) dx masturbation problem by a psychiatrist; (4) masturbates as a daily habit **Exclusion criteria:** (1) any condition that would interfere with the safe study participation; (2) any current neurological or axis I psychiatric disorders that needs chronic drug treatment; (3) treated for masturbation in the last month; (4) infection of genitalia.	**N:** 42 **Age, mean±SD (range):** 5.3±1.1 **Males %:** 52.3 **Caucasian %:** NR **Diagnostic breakdown (n):** **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 2** **N:** 45 **Age, mean±SD (range):** 49.9±1.1 **Males %:** 57.7 **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR	**(range):** NR **Concurrent treatments:** NR **GROUP 2** **Drug name:** placebo **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR		group, the addition of risperidone to the behavioral treatment was effective in all ages.
Owen et al., 2009 [61] **Country:** USA **Condition category:** ASD **Funding:** Industry **Risk of bias:** Medium (subjective), Low (objective)	**Recruitment dates:** June 2006 to April 2008 **Study design:** RCT (parallel) **Setting:** NR **Diagnostic criteria:** DSM-IV-TR, ADI-R, CGI-S, ABC-I **Inclusion criteria:** (1) 6–17 yr, (2) DSM-IV-	**Enrolled:** 164 **Analyzed:** 98 **Completed:** 75 **GROUP 1** **N:** 47 **Age, mean±SD (range):** 9.7±3.2 **Males %:** 89.4 **Caucasian %:** 68.1 **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NA	**Treatment duration:** 8 wk **Run-in phase:** Yes **Run-in phase duration:** ≤6 wk **Permitted drugs:** anxiolytics, benztropine or propranolol, diphenhydramine (≤50 mg/day), psychotropic medication, sleep aids **Prohibited drugs:** antidepressants, antipsychotics, anxiolytics, mood stabilizers, neuroleptics, psychostimulants (washout ≥4 day), fluoxetine, olanzapine/fluoxetine (washout ≥4 wk before screen visit)	**Benefits:** ABC, CYBOCS, CGI-I, CGI-S, PedsQL, CGSQ, response (ABC-I, CGI-I), suicide **Harms:** EPS (AIMS, BAS, SAS), fatigue, glucose, lipid profile, prolactin, LDL, total cholesterol, HDL, somnolence, aggression, total AE, weight change	During an 8-week period, aripiprazole was efficacious and generally well tolerated in the treatment of irritability associated with autistic disorder in children and adolescents who may be experiencing tantrums, aggression, self-injurious behavious, or a combination

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	TR criteria for autistic disorder and behaviors such as tantrums, aggression, self–injury, or a combination, with a dx corroborated by ADI-R certified trainer, (3) CGI-S score ≥4 and ABC Irritability subscale score ≥18 at screening and baseline, (4) ≥15 kg, (5) stable nonpharmacologic therapy **Exclusion criteria:** (1) bipolar disorder, psychosis, schizophrenia, major depression, fragile X syndrome, or another ASD, (2) history of NMS, (3) significant risk of committing suicide, (4) seizure in the past yr, (5) history of severe head trauma or stroke, (6) history or current evidence of any unstable medical condition or or an abnormal laboratory test result considered clinically significant, (7) antipsychotic treatment resistant, (8) known allergy or hypersensitivity to aripiprazole	**GROUP 2** **N:** 51 **Age, mean±SD (range):** 8.8±2.6 **Males %:** 86.3 **Caucasian %:** 80.4 **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NA	**GROUP 1** **Drug name:** Aripiprazole **Dosing variability:** flexible **Target dose (mg/day):** 5, 10, 15 **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** analgesics and antipyretics hypnotics and sedatives **GROUP 2** **Drug name:** Placebo **Dosing variability:** flexible **Target dose (mg/day):** 5, 10, 15 **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** analgesics and antipyretics, hypnotics and sedatives		ofthese symptoms.
Pandina et al., 2007 [124]	**Study design:** Observational (pooled	**Enrolled:** NA **Analyzed:** 228	**GROUP 1** **Drug name:** Risperidone	**Benefits:** continuous performance task	Cognitive function was not altered by

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
(see Aman 2002, Snyder 2002) **Country:** Canada, South Africa, USA **Condition category:** ADHD **Funding:** NR **Newcastle-Ottawa Scale:** 6/8 stars	analysis)	**Completed:** NA **GROUP 1** **N:** 108 **Age, mean±SD (range):** 8.6 yr **Males %:** 81 **Caucasian %:** 64 **Diagnostic breakdown (n):** CD (40), ODD (29), Axis 1 (34), BD NOS (5) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (78) **GROUP 2** **N:** 88 **Age, mean±SD (range):** 8.4 yr **Males %:** 77 **Caucasian %:** 68 **Diagnostic breakdown (n):** CD (48), ODD (30), Axis 1 (37), BD NOS (5) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (77)	**Dosing variability:** Variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.3±0.7 mg/day **Concurrent treatments:** See Aman 2002 and Snyder 2002 **GROUP 2** **Drug name:** Placebo **Dosing variability:** Variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** See Aman 2002 and Snyder 2002	(CPT), VLT-C **Harms:** NA	risperidone in short term studies.
Pathak et al., 2013 [62] **Country:** USA **Condition category:** Bipolar I (manic)	**Recruitment dates:** Aug 2004 to Jul 2006 **Study design:** RCT (parallel) **Setting:** Inpatient/outpatient	**Enrolled:** 284 **Analyzed:** 277 **Completed:** 222 **GROUP 1** **N:** 93 **Age, mean±SD (range):** 13.1±2.2 **Males %:** 50.5	**Treatment duration:** 3 wk **Run–in phase:** Yes **Run–in phase duration:** 1–28 day **Permitted drugs:** Psychostimulants, diphenhydramine, hydroxyzine, lorazepam, benztropine	**Benefits:** CGAS, CGI-BP-S, CGI-BP-I, YMRS,CDRS-R, OAS-M, CGSQ, response, remission, suicidal ideation, aggression, bipolar disorder exacerbation	Quetiapine at 400 mg/d and 600 mg/d was significantly more effective than placebo for treating acute manic symptoms in youth with bipolar I disorder. Quetiapine

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Funding: Industry **Risk of bias:** High (subjective), High (objective)	**Diagnostic criteria:** DSM-IV, KID-SCAD-PL **Inclusion criteria:** (1) Male and female inpatients and outpatients, (2) aged 10 to 17 years, (3) DSM-IV diagnosis of Bipolar I mania as confirmed by K-SADS-PL, (4) YMRS total score of ≥20 at both screening and randomization, (5) permitted to have secondary diagnosis of ADHD **Exclusion criteria:** (1) Current DSM-IV-diagnosed Axis I disorder other than bipolar I disorder or ADHD, (2) history of serious suicide attempts, (3) current risk for suicide or homicide in the judgment of investigators	**Caucasian %:** 78.5 **Diagnostic breakdown (n):** manic (92), mixed (1) **Treatment naïve (n):** 68 **Inpatients (n):** NR **First episode psychosis (n):** 6 **Comorbidities:** ADHD (49) **GROUP 2** **N:** 95 **Age, mean±SD (range):** 13.2±2.2 **Males %:** 57.9 **Caucasian %:** 76.8 **Diagnostic breakdown (n):** manic (91), mixed (4) **Treatment naïve (n):** 79 **Inpatients (n):** NR **First episode psychosis (n):** 6 **Comorbidities:** ADHD (40) **GROUP 3** **N:** 89 **Age, mean±SD (range):** 13.3±2.1 **Males %:** 60.7 **Caucasian %:** 74.2 **Diagnostic breakdown (n):** manic (all) **Treatment naïve (n):** 74 **Inpatients (n):** NR **First episode psychosis (n):** 7 **Comorbidities:** ADHD (35)	**Prohibited drugs:** Prophylactic use of benztropine **GROUP 1** **Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** 400 **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 2** **Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** 600 **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 3** **Drug name:** Placebo **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	**Harms:** EPS (AIMS, BAS, SAS), akathisia, mortality, weight gain, somnolence, fatigue, glucose measures, lipid values, liver function, thyroid function, prolactin, tachycardia, pulse, heart rate, ECG changes, hematology values,	at these doses was generally well tolerated and AE were consistent with the profile of quetiapine in adults with bipolar disorder.
Perry et al., 1989 [63] **Country:** USA	**Recruitment dates:** NR	**Enrolled:** 70 **Analyzed:** 60 **Completed:** 52	**Treatment duration:** 6 mo **Run-in phase:** Yes **Run-in phase duration:** 2 wk	**Benefits:** CGI-I, Response (CGI-I, CGI-S)	Haloperidol, administered on a long-term basis,

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Condition category: ASD **Funding:** Industry, Government, Foundation **Risk of bias:** High (subjective), High (objective)	**Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-III-TR **Inclusion criteria:** (1) dx of infantile autism, full syndrome present, (2) only children with good response to haloperidol and requiring further drug treatment were accepted into the study **Exclusion criteria:** (1) identifiable cause for autism, (2) seizure disorder, (3) preexisting movement disorder	**GROUP 1** **N:** 34 **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 2** **N:** 36 **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR	**Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Haloperidol (continuous) **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.2 (0.5–4) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Haloperidol (discontinuous) **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1 (0.5–4.0) **Concurrent treatments:** NR	**Harms:** Dyskinesia, parkinsonism, sedation	effectively reduced maladaptive symptoms in austic children. Drug efficacy was not deminished by discontinuous drug administration.
Pogge et al., 2005 [125] **Country:** USA **Condition category:** Mixed conditions **Funding:** NR **Newcastle-Ottawa Scale:** 6/8 stars	**Recruitment dates:** NR **Study design:** Prospective **Setting:** Inpatient **Diagnostic criteria:** NR **Inclusion criteria:** All adolescent inpatients discharged from a private psychiatric hospital during a 2 yr period who received 1	**Enrolled:** 86 **Analyzed:** 86 **Completed:** 86 **GROUP 1** **N:** 43 **Age, mean±SD (range):** See below **Males %:** See below **Caucasian %:** See below **Diagnostic breakdown (n):** Depressive disorder (11), mood disorder NOS (10), SUD (8), DBD (7), psychotic disorder (9), anxiety disorder (7), BP (8), ADHD (4), ED (1)	**Treatment duration:** 12 wk -18 mo follow up **Run-in phase:** NA **Run-in phase duration:** NA **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	**Benefits:** NA **Harms:** Weight	The general lack of significant relationships between symptoms or diagnosis, other than substance abuse, and non adherence is not surprising, given heterogeneity of the sample and the general tendencies toward non adherence on the part of adolescents with both medical and psychiatric

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	of the medications (olanzapine, risperidone) as an inpatient and a follow up prescription **Exclusion criteria:** NR	**Treatment naïve (n):** 0 **Inpatients (n):** 43 **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 43 **Age, mean±SD (range):** See below **Males %:** See below **Caucasian %:** See below **Diagnostic breakdown (n):** Depressive disorder (26), mood disorder NOS (7), SUD (7), DBD (8), psychotic disorder (3), anxiety disorder (5), BP (2), ADHD (3), ED (1) **Treatment naïve (n):** 0 **Inpatients (n):** 43 **First episode psychosis (n):** NR **Comorbidities:** NR **Overall age, mean±SD (range):** 14.9±1.3 yr **Overall males %:** 41.9 **Overall Caucasian %:** 65.1	**GROUP 2** **Drug name:** Risperidone **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR		conditions.
Ratzoni et al., 2002 [126] **Country:** Israel **Condition category:** Schizophrenia and related **Funding:**	**Recruitment dates:** Jan 2000 to Aug 2000 **Study design:** Prospective cohort **Setting:** Inpatient **Diagnostic criteria:** DSM-IV, K-SADS-PL (Hebrew version),	**Enrolled:** 50 **Analyzed:** 50 **Completed:** 36 **GROUP 1** **N:** 8 **Age, mean±SD (range):** 17.3±1.3 (15–19) **Males %:** 62.5 **Caucasian %:** NR **Treatment naïve (n):** 1	**Treatment duration:** 2.8 mo **Run-in phase:** Yes **Run-in phase duration:** 5.2 day (mean) **Permitted drugs:** anticholinergics, lorazepam **Prohibited drugs:** antipsychotics, heterocyclic antidepressants, lithium, medications that can cause	**Benefits:** PANSS, medication adherence **Harms:** Akathisia, behavioral issues, BMI, constipation, dermatologic AE, dystonia, any EPS, fatigue, hypokinesia-akinesia, sedation,	Adolsecents experienced greater weight gain when taking olanzapine or risperidone compared to effects reported in adults.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Government, Foundation **Newcastle-Ottawa Scale:** 3/8 stars	consensus of 2 child psychiatrists **Inclusion criteria:** (1) adolescent patients who started treatment with olanzapine, risperidone, or haloperidol from Jan to Aug 2000 **Exclusion criteria:** (1) receiving other medications that cause weight gain/loss, (2) alcohol/substance abuse, (3) medical illnesses affecting body weight	**Inpatients (n):** all **First episode psychosis (n):** NR **GROUP 2** **N:** 21 **Age, mean±SD (range):** 17±1.6 (14–19) **Males %:** 66.7 **Caucasian %:** NR **Treatment naïve (n):** 2 **Inpatients (n):** all **First episode psychosis (n):** NR **GROUP 3** **N:** 21 **Age, mean±SD (range):** 17.1±2.1 (13–20.5) **Males %:** 57.1 **Caucasian %:** NR **Treatment naïve (n):** 3 **Inpatients (n):** all **First episode psychosis (n):** NR	weight gain/loss, SSRIs, valproic acid **GROUP 1** **Drug name:** Haloperidol **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 7.6±4 (3–15) **Concurrent treatments:** biperiden (6), lorazepam (5), trihexyphenidyl (2) **GROUP 2** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 12.7±3.1 (7.5–20) **Concurrent treatments:** biperiden (6), lorazepam (5), trihexyphenidyl (2) **GROUP 3** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 3.2±1.1 (1–5) **Concurrent treatments:** biperiden (6), lorazepam (5), trihexyphenidyl (2)	seizure, sexual desire, tachycardia, WAE, weight	
Remington et al., 2001 [64] **Country:** Canada **Condition category:** ASD **Funding:** Non-industry	**Recruitment dates:** NR **Study design:** RCT (crossover) **Setting:** NR **Diagnostic criteria:** DSM-IV	**Enrolled:** 37 **Analyzed:** 33 **Completed:** 23/33 (H), 12/32 C, 21/32 (P) **GROUP 1** **N:** 33 **Age, mean±SD (range):** 16.3 (10–36) yr **Males %:** 83.3	**Treatment duration:** 7 wk **Run-in phase:** Yes **Run-in phase duration:** 1 wk before and between each arm of the treatment regimen **Permitted drugs:** benztropine **Prohibited drugs:** no other antipsychotic medications	**Benefits:** ABC, CARS **Harms:** fatigue, ESRS, dystonia, depression, ECG, arrythmias	Results favor haloperidol over clomipramine in the treatment of autistic disorder. The two agents demonstrated comparable improvement when compared with

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Caucasian %: NR			baseline if there was a full therapeutic trial; however, significantly fewer individuals treated with clomipramine were able to do this, for reasons related both to side effects and efficacy.
Risk of bias: High (subjective), High (objective)	**Inclusion criteria:** (1) DSM-IV diagnosis of autism confirmed independently bt two investigators, (2) evidence that haloperidol or clomipramine had not been used previously, or, if so, that an adequate therapeutic trial was not completed **Exclusion criteria:** NR	**Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR	**GROUP 1** **Drug name:** Chlomipramine-Placebo-Haloperidol (CPH), PHC, HCP **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1-1.5 **Concurrent treatments:** NR		
Reyes et al., 2006 [65] **Country:** Belgium, Germany, Great Britain, Israel, Netherlands, Poland, South Africa, Spain **Condition category:** ADHD **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** Aug 2001 to Sep 2003 **Study design:** RCT (parallel) **Setting:** NR **Diagnostic criteria:** DSM-IV, K-SADS-PL **Inclusion criteria:** (1) 5–17 yr, (2) no moderate or severe intellectual impairment (IQ ≥55), (3) CD serious enough to warrant clinical treatment, (4) score ≥24 on the conduct problem subscale of the NCBRF, (5) responsible caregiver **Exclusion criteria:** (1) schizophrenia and	**Enrolled:** 335 **Analyzed:** 335 **Completed:** 162 **GROUP 1** **N:** 172 **Age, mean±SD (range):** 10.9±2.9 **Males %:** 82 **Caucasian %:** NR **Diagnostic breakdown (n):** CD (62), DBD NOS (3), ODD (107) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (117) **GROUP 2** **N:** 163 **Age, mean±SD (range):** 10.8±2.9 **Males %:** 91 **Caucasian %:** NR	**Treatment duration:** 7.4 mo **Run-in phase:** Yes **Run-in phase duration:** 6 wk **Permitted drugs:** medication for EPS (only after dose reduction attempted), psychostimulants **Prohibited drugs:** anticonvulsants, antidepressants, antipsychotics, lithium **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 0.8±0.3 (<50 kg), 1.2±0.4 (≥50 kg) **Concurrent treatments:** analgesics (26), psychostimulants (36) **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR	**Benefits:** CGAS, CGI-I, CGI-S, NCBRF, VAS-MS Cognitive (MVLT, CPT), growth (tannar stages), response (relapse, symptom recurrence) **Harms:** Akathisia, BMI, dystonia, EPS, fatigue, parkinsonism, prolactin, prolactin-related AE, SAE, somnolence, tardive dyskinesia, total AE, WAE, weight change	Patients who responded to initial treatment with risperidone benefited from continued, long-term treatment. Risperidone was safe and well tolerated during a 1-year extension.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	bipolar disorder	**Diagnostic breakdown (n):** CD (61), DBD NOS (5), ODD (97) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (110)	**Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** analgesics (20), psychostimulants (36)		
Rizzo et al., 2012 [66] **Country:** Italy **Condition category:** Tic disorders **Funding:** Non-industry **Risk of Bias:** High (subjective), High (objective)	**Recruitment Dates:** NR **Study design:** NRCT (parallel) **Diagnostic criteria:** DSM-IV-TR **Setting:** Outpatients **Inclusion criteria:** TS according to DSM-IV-TR, from Neurology Unit of Catania University **Exclusion criteria:** NR	**Enrolled:** 75 **Analyzed:** 75 **Completed:** 75 **GROUP 1:** **N:** 25 **Age, mean±SD (range):** 11.6 ±2.2 yr **Males %:** 88% **Caucasian %:** NR **Diagnostic breakdown (n):** Tourette syndrome (25) **Treatment naïve (n):** (1) **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** OCD (11), ADHD (3) **GROUP 2:** **N:** 25 **Age, mean±SD (range):** 11.2±3.1 yr **Males %:** 92% **Caucasian %:** NR **Diagnostic breakdown (n):** Tourette syndrome (25) **Treatment naïve (n):** (22) **Inpatients (n):** NR **First episode psychosis (n):** NR	**Treatment duration:** 24 mo **Run-in phase:** Yes **Run-in phase duration:** 4 wk **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Aripiprazole **Dosing variability:** Variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.25-15 mg/day **Concurrent treatments:** Fluoxetine (10), Biperiden cloridrate (7) **GROUP 2:** **Drug name:** Pimozide **Dosing variability:** Variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1-4 mg/day **Concurrent treatments:** Fluoxetine (7), Biperiden cloridrate (12) **GROUP 3:** **Drug name:** No medication **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	**Benefits:** NR **Harms:** BMI, glycemia, triglyceridemia, cholesterolemia	Pimozide and aripiprazole have slightly different contraindications for use in children with Tourette syndrome. Pimozide may be less well-suited to diabetic patients. Patients with predisposition to cholesterol problems may require closer monitoring when taking aripiprazole.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Comorbidities (n): OCD (9), ADHD (5) **GROUP 3:** **N:** 25 **Age, mean±SD (range):** 10.2±2.8 yr **Males %:** 88% **Caucasian %:** NR **Diagnostic breakdown (n):** Tourette syndrome (25) **Treatment naïve (n):** (25) **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** OCD (0), ADHD (2)			
RUPP et al., 2005 [67] **Country:** USA **Condition category:** ASD **Funding:** Industry/ Non-industry **Risk of bias:** Medium (subjective), Medium (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** NR **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) responders at the end of 4 mo extension study. For initial inclusion criteria refer to McCracken 2002 **Exclusion criteria:** NR. For initial exclusion criteria refer to McCracken 2002	**Enrolled:** 38 **Analyzed:** NR **Completed:** 32 **GROUP 1** **N:** 16 **Age, mean±SD (range):** see below **Males %:** see below **Caucasian %:** see below **Diagnostic breakdown (n):** NR **Treatment naïve (n):** see below **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** see below **GROUP 2** **N:** 16 **Age, mean±SD (range):**	**Treatment duration:** 8 wk **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** anticonvulsant treatment if child had been taking stable dose for 4 wk and had been free of seizures for 6 mo **Prohibited drugs:** other psychotropic medication **GROUP 1** **Drug name:** Risperidone **Dosing variability:** fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 3.5 (15-45 kg), 4.5 (>45 kg) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable	**Benefits:** Relapse, ABC **Harms:** NR	Risperidone showed persistent efficacy and good tolerability for intermediate-length treatment of children with autism characterized by tantrums, aggression, and/or self-injurious behavior. Discontinuation after 6 months was associated with a rapid return of disruptive and aggressive behavior in most subjects.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		see below **Males %:** see below **Caucasian %:** see below **Diagnostic breakdown (n):** NR **Treatment naïve (n):** see below **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** see below **Overall age, mean±SD (range):** 9.0±2.5 yr **Overall males %:** 86.8 **Caucasian %:** 60.5 **Overall treatment naïve (n):** 7 **Overall comorbidities:** IQ average (2), IQ borderline (5), MR (27)	**Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 25% dosage reduction/wk **Concurrent treatments:** NR		
Saito et al., 2004 [127] **Country:** USA **Condition category:** Mixed conditions **Funding:** Government **Newcastle-Ottawa Scale:** 6/8 stars	**Recruitment dates:** Sept 2001 to Mar 2003 **Study design:** Prospective cohort **Setting:** Inpatient/outpatient **Diagnostic criteria:** NR **Inclusion criteria:** (1) male and females, (2) aged 5 to 18 years, (3) treatment naïve or at least a 1-month interval since their last treatment with antipsychotic agents,	**Enrolled:** 40 **Analyzed:** 40 **Completed:** 40 **GROUP 1** **N:** 13 **Age, mean±SD (range):** all groups: 13.4±3.4 (5–18) **Males %:** all groups: 55 **Caucasian %:** NR **Diagnostic breakdown (n):** all groups: schizophrenia or other psychosis (14), mood disorders (14), DBD (9), intermittent explosive disorder (1), PDD NOS (1), eating disorder NOS (1)	**Treatment duration:** 11.2 wk **Run–in phase:** Yes **Run–in phase duration:** 1 mo. **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 7.8±4.2 **Concurrent treatments:** all groups: divalproex sodium (7), lithium (5), SSRI (11), stimulants (9), benzodiazepines (3), alpha-adrenergic agonists (3)	**Benefits:** NA **Harms:** prolactin, prolactin-related AEs	Prolactin levels were significantly increased in children and adolescents treated with risperidone, compared to those treated with olanzapine or quetiapine.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	(4) inpatients or outpatients at a suburban children's hospital **Exclusion criteria:** (1) females receiving hormonal contraception	**Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** NR **GROUP 2** **N:** 6 **Age, mean±SD (range):** see group 1 **Males %:** see group 1 **Caucasian %:** NR **Diagnostic breakdown (n):** see group 1 **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** NR **GROUP 3** **N:** 21 **Age, mean±SD (range):** see group 1 **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown (n):** see group 1 **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** NR	**GROUP 2** **Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 283.3±222.9 **Concurrent treatments:** see group 1 **GROUP 3** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 2.2±2 **Concurrent treatments:** see group 1		
Sallee et al., 2000 [70] **Country:** USA **Condition category:** Tic disorders	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Outpatient/community	**Enrolled:** 28 **Analyzed:** 27 **Completed:** 24 **GROUP 1** **N:** 16 **Age, mean±SD (range):** 11.3 (7–14)	**Treatment duration:** 8 wk **Run-in phase:** Yes **Run-in phase duration:** 4–8 wk **Permitted drugs:** NR **Prohibited drugs:** NR	**Benefits:** CGI-TS, CYBOCS, YGTSS **Harms:** Akathisia, prolactin, prolactin-related AESAE, sedation, somnolence, total AE,	Ziprasidone was well tolerated in children and adolscents with Tourette syndrome, and may also be an effective anti-tic medication.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Males %: 87.5 **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (9), DBD (4), OCD (10; all groups), learning disability (2; all groups) **GROUP 2** **N:** 12 **Age, mean±SD (range):** 11.8 (8–16) **Males %:** 66.7 **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (6), DBD (1), OCD (10; all groups), learning disability (2; all groups)	**GROUP 1** **Drug name:** Ziprasidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 28.2±9.6 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	WAE, weight change	
Sallee et al., 1997 [69] **Country:** USA **Condition category:** Tic disorders **Funding:** Industry, Government **Risk of bias:** High	**Recruitment dates:** NR **Study design:** RCT (crossover) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-III-TR, K-SADS-P **Inclusion criteria:** (1)	**Enrolled:** 22 **Analyzed:** 22 **Completed:** 22 **GROUP 1** **N:** 22 (crossover) **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR	**Treatment duration:** 6 wk **Run-in phase:** Yes **Run-in phase duration:** >2 wk **Permitted drugs:** diphenhydramine hydrochloride **Prohibited drugs:** adjunctive treatment, anticholinergics, concomitant medications **GROUP 1** **Drug name:** Haloperidol	**Benefits:** CGAS, CGI-S Medication adherence, response **Harms:** Akathisia, akinesia, behavioral issues, electrocardiovascular, EPS (AIMS, ESRS), prolactin, treatment limiting AE, WAE, weight change	Pimozide is superior to haloperidol for controlling symptoms of Tourette syndrome in children and adolescents.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
(subjective), High (objective)	principal DSM-III-R dx of Tourette syndrome; may have multiple Axis I and II dx, (2) 7–16 yr, 11 mo, (3) TSGS score >20, (4) previous exposure to neuroleptics permitted, but treatment must have been withdrawn ≥2 wk before baseline **Exclusion criteria:** (1) chronic motor tic disorder or transient tic disorder, (2) serious medical illness, (3) abnormal ECG, (4) inability to perform required measurements, (5) use of concurrent medication that may alter or interact with haloperidol or pimozide, (6) history of drug or alcohol abuse, (7) autism or childhood schizophrenia	**Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (13), OCD (5) **GROUP 2** **N:** 22 (crossover) **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** see G1 **GROUP 3** **N:** 22 (crossover) **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** see G1	**Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 3.5±2.2 (1–8) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Pimozide **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 3.4±1.6 (1–6) **Concurrent treatments:** NR **GROUP 3** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR		
Sallee et al., 1994 [68] **Country:** USA **Condition category:** Tic disorders	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Outpatient/community	**Enrolled:** 41 **Analyzed:** 41 **Completed:** NR **GROUP 1** **N:** 17 **Age, mean±SD (range):** 10.4 **Males %:** NR	**Treatment duration:** 6 wk **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1**	**Benefits:** CBCL-TRF, cognitive (CPT, MST) **Harms:** NR	The effect of pimozide treatment on cognotion was superior to haloperidol in children with Tourette syndrome with comorbid ADHD.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Funding: Foundation **Risk of bias:** Medium (subjective), Medium (objective)	**Diagnostic criteria:** DSM-III-TR, TSGS **Inclusion criteria:** (1) consecutive outpatient children who met DSM-III-R criteria for Tourette syndrome and severity criteria using the TSGS **Exclusion criteria:** NR	**Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (6) **GROUP 2** **N:** 24 **Age, mean±SD (range):** 10.8 **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (7)	**Drug name:** Haloperidol **Dosing variability:** fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.5±0.6 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Pimozide **Dosing variability:** fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 3.7±1.4 **Concurrent treatments:** NR		
Savitz et al., 2015 [71] **Country:** India, Romania, Russia, Slovakia, Spain, Ukraine, and the United States **Condition category:** Schizophrenia and related **Funding:** Industry **Risk of bias:** Medium (subjective), Medium (objective)	**Recruitment dates:** November 2009 to June 2012 **Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) 12-17 yr, (2) body weight ≥ 29kg, (3) diagnosis of schizophrenia ≥1yr, (4) Positive and Negative Symptom Score	**Enrolled:** 228 **Analyzed:** 226 **Completed:** 174 **GROUP 1** **N:** 112 **Age, mean±SD (range):** 15.2±1.5 **Males %:** 65 **Caucasian %:** 75 **Treatment naïve (n):** 13 **Inpatients (n):** 70 (at screening) **First episode psychosis (n):** 0 **GROUP 2** **N:** 114 **Age, mean±SD (range):** 15.4±1.5	**Treatment duration:** 8wk acute, 18 wk maintenance **Run-in phase:** Yes **Run-in phase duration:** ≤3 wks **Permitted drugs:** antidepressants, certain benzodiazepines, and non-benzodiazepine hypnotics; anticholinergics, topical antifungal agents, antihistamines, anti-inflammatory drugs except systemic corticosteroids, histamine-2 (H2) blockers, and rescue medications for the treatment of restlessness, agitation, insomnia, or extrapyramidal symptoms **Prohibited drugs:** antipsychotics, psychostimulants or other dopamine agonists, certain sedatives	**Benefits:** PANSS, maintenance of stability, CGI-S, response **Harms:** AIMS, BAS, SAS, any AE, C-SSRS, prolactin, weight, ECG, glucose, insulin, lipids	Palirperidone ER did not demonstrate superiority to aripiprazole in treating adolescent schizophrenia.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	(PANSS) total score of 60 to 120 (inclusive) at screening, (5) ≥1 prior adequate treatment with antipsychotic medication, (6) clinician belief that suboptimnal current treatment **Exclusion criteria:** (1) diagnosis of BD, MDD, schizoaffective disorder, schizophreniform disorder, ASD, MR, primary substance-induced psychotic disorder, dissociative disorder or SUD in 3 months before screening, (2) history of seizure disorder, neuroleptic malignant syndrome, encephalopathic syndrome, tardive dyski-nesia, or insulin-dependent diabetes mellitus, (3) receiving clozapine (2 months before screening), (4) depot antipsychotic therapy within 2 treatment cycles before screening, or electroconvulsive therapy (3 months before baseline visit), (5) sexually	**Males %:** 67 **Caucasian %:** 77 **Treatment naïve (n):** 11 **Inpatients (n):** 68 (at screening) **First episode psychosis (n):** 0	(including barbiturates), hypnotics, or anxiolytics, mood stabilizers or anticonvulsants, electroconvulsive therapy, inhibitors or inducers of CYP3A4 or CYP2D6 **GROUP 1** **Drug name:** Paliperidone ER **Dosing variability:** variable **Target dose (mg/day):** 6 mg per day [days 1–7], flexibly dosed 3, 6, or 9mg per day from day 8 to end of study [EOS] **Daily dose (mg/day), mean±SD (range):** 6.75±1.8 **Concurrent treatments:** anti-EPS medications or antihistamines (26%) **GROUP 2** **Drug name:** Aripiprazole **Dosing variability:** variable **Target dose (mg/day):** 2 mg per day ([days 1 and 2], 5 mg per day [days 3 and 4], 10 mg per day [days 5–7], flexibly dosed 5, 10, or 15 mg per day from day 8 to EOS **Daily dose (mg/day), mean±SD (range):** 11.6±3.0 **Concurrent treatments:** anti-EPS medications or antihistamines (25%)		

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	nonabstinent girls who were pregnant, nursing, or of childbearing capacity.				
Scahill et al., 2003 [72] **Country:** USA **Condition category:** Tic disorders **Funding:** Industry, Government **Risk of bias:** Medium (subjective), Medium (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV, joint parent and child interview **Inclusion criteria:** (1) 7–65 yr, (2) Tourette syndrome (DSM-IV), (3) Total Tic score ≥22 on the YGTSS **Exclusion criteria:** (1) evidence of current major depression, GAD, separation anxiety disorder, or psychotic symptoms (clinical evaluation or DSM-IV), (2) WISC age-appropriate IQ <70, (3) prior adequate trial of risperidone (dose ≥1.0 mg/day for ≥2 wk), (4) psychotropic medication within 2 wk, (5) significant medical problem, (6) moderate or greater obsessive-compulsive symptoms	**Enrolled:** 26 **Analyzed:** 26 **Completed:** NR **GROUP 1** **N:** 12 **Age, mean±SD (range):** 11.1 (2.20) yrs (whole pediatric sample) **Males %:** 96% (whole pediatric sample) **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (11), MR (0), OCD (4) **GROUP 2** **N:** 14 **Age, mean±SD (range):** See group 1 **Males %:** see group 1 **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** see group 1	**Treatment duration:** 8 wk **Run-in phase:** Yes **Run-in phase duration:** 1–2 wk **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** 3 **Daily dose (mg/day), mean±SD (range):** 2.5±0.9 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** 3 **Daily dose (mg/day), mean±SD (range):** 3.3±0.9 **Concurrent treatments:** NR	**Benefits:** CGI-I, YGTSS Response **Harms:** Weight, EPS, social phobia	For short-term treatment of tics in children, risperidone appeared to be safe and effective.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	(YBOCS>15)				
Schneider et al., 2012 [73] **Country:** USA **Condition category:** Bipolar I (manic, mixed) **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** NR **Diagnostic criteria:** DSM-IV-TR, K-SADS-PL **Inclusion criteria:** (1) 10-17 yr, (2) DSM-IV-TR bipolar I disorder confirmed with K-SADS-PL, (3) YMRS score ≥16 at both screening and baseline **Exclusion criteria:** (1) dx of substance abuse or dependence in the previous month for any substance other than nicotine or caffeine, (2) being clinically stable on a well-tolerated treatment regimen, (3) prior treatment with ziprasidone, a known allergy to ziprasidone, or a serious suicidal risk, (4) any history of head injury resulting in loss of consciousness for > 10 minutes, or any unstable medical or neurological disorder.	**Enrolled:** 23 **Analyzed:** 17 **Completed:** 11 **GROUP 1** **N:** 14 **Age, mean±SD (range):** 14.7±2.3 yr **Males %:** 64 **Caucasian %:** 86 **Diagnostic breakdown (n):** mixed (9) **Treatment naïve (n):** see below **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (3) **GROUP 2** **N:** 9 **Age, mean±SD (range):** 14.5±2.2 yr **Males %:** 22 **Caucasian %:** 89 **Diagnostic breakdown (n):** mixed (9) **Treatment naïve (n):** see below **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (7) **Overall Treatment naïve (n):** 7	**Treatment duration:** 4 wk **Run-in phase:** Yes **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Ziprasidone **Dosing variability:** variable **Target dose (mg/day):** ≥45kg: 120-160, <45kg: 60-80 **Daily dose (mg/day), mean±SD (range):** 20 [initial dose] **Concurrent treatments:** all groups: benztropine (1), lorazepam (1) **GROUP 2** **Drug name:** Placebo **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	**Benefits:** YMRS, response, medication adherence **Harms:** NR	Further research is needed to determine whether treatment related increases in ventral prefrontal activation are associated with improvements in sustained attention and other executive function domains, if there are differences in patterns of change patients experiencing manic versus mixed episodes, as well as to investigate whether func-tional alterations in specific regions of ventral prefrontal cortex may be useful as specific biomarkers of ziprasidone response in patients with mania.
Sehgal et al., 1999	**Recruitment dates:**	**Enrolled:** 10	**Treatment duration:** 8 mo	**Benefits:**	In children with

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
[74]	Oct 1993 to Nov 1995	**Analyzed:** 10 **Completed:** 8	**Run-in phase:** Yes **Run-in phase duration:** 4 mo	Response	Tourette syndrome, longer term treatment with pimozide appears to be more effective on the course of tics than a short-term course of the drug used to suppress an acute exacerbation of tics.
Country: USA	**Study design:** RCT (parallel)	**GROUP 1** **N:** 4	**Permitted drugs:** NR	**Harms:** Tardive dyskinesia, sedation	
Condition category: Tic disorders	**Setting:** NR	**Age, mean±SD (range):** NR	**Prohibited drugs:** antidepressants, benzodiazepines, clonidine, stimulants (washout ≥2 wk prior to enrolment)		
Funding: Industry, Government, Foundation	**Diagnostic criteria:** DSM-III-TR	**Males %:** NR **Caucasian %:** NR **Diagnostic breakdown (n):** NR	**GROUP 1**		
Risk of bias: Medium (subjective), NA (objective)	**Inclusion criteria:** (1) DSM-III-R diagnostic criteria for Tourette syndrome at participating medical centers	**Treatment naïve (n):** all **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** NR	**Drug name:** Pimozide (short-term) **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 3. 8 (2–6) **Concurrent treatments:** NR		
	Exclusion criteria: NR	**GROUP 2** **N:** 6 **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** all **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** NR	**GROUP 2** **Drug name:** Pimozide (long-term) **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 3.5 (1–7) **Concurrent treatments:** NR		
Shaw et al., 2006 [75]	**Recruitment dates:** Jan 1998 to June 2005	**Enrolled:** 25 **Analyzed:** 25 **Completed:** 24	**Treatment duration:** 8 wk **Run-in phase:** Yes **Run-in phase duration:** 3 wk	**Benefits:** BPRS-24, CGI-S, SANS, SAPS, response	Clozapine had a more favorable profile of clinical response and adverse events than olanzapine.
Country: USA	**Study design:** RCT (parallel)	**GROUP 1** **N:** 12	**Permitted drugs:** NR	**Harms:** Behavioral issues, blood cells, blood pressure, constipation, dermatologic AE, ECG changes, STESS, AIMS, SAS, lipid profile, seizure,	
Condition category: Schizophrenia and related	**Setting:** Inpatient	**Age, mean±SD (range):** 11.7±2.3	**Prohibited drugs:** NR		
Funding: NR	**Diagnostic criteria:** DSM-IV, K-SADS, medical and school record review,	**Males %:** 66.7 **Caucasian %:** 58.3 **Treatment naïve (n):** 0 **Inpatients (n):** all	**GROUP 1** **Drug name:** Clozapine **Dosing variability:** variable **Target dose (mg/day):** NR		

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Risk of bias: Medium (subjective), Medium (objective)	interview with child and parents **Inclusion criteria:** (1) schizophrenia with definite onset of symptoms ≤13 yr , (2) IQ >70, (3) no history of progressive neurological or medical disorders, (4) failure to respond to 2 antipsychotic medications (typical or atypical) used at adequate doses (>100 mg chlorpromazine equivalents) and for adequate duration (>4 wk unless terminated owing to intolerable adverse effects) **Exclusion criteria:** (1) nonresponse to an adequate trial of olanzapine or clozapine (8 wk of olanzapine at 20 mg/d or of clozapine at 200 mg/d)	**First episode psychosis (n):** 0 **Comorbidities:** ADHD (4), anxiety disorders (6), MR (0) **GROUP 2** **N:** 13 **Age, mean±SD (range):** 12.8±2.4 **Males %:** 53.8 **Caucasian %:** 53.8 **Treatment naïve (n):** 0 **Inpatients (n):** all **First episode psychosis (n):** 0 **Comorbidities:** ADHD (3), anxiety disorders (1), MR (0)	**Daily dose (mg/day), mean±SD (range):** 327±113 (150–500) **Concurrent treatments:** diphenhydramine hydrochloride (4), guanfacine hydrochloride (1), lorazepam (2), sedatives (4), ≤4 hr specialized education, recreational and occupational therapy **GROUP 2** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 18.1±4.3 **Concurrent treatments:** clomipramine hydrochloride (1), diphenhydramine hydrochloride (6), lorazepam (3), sedatives (3), valproate sodium (2), ≤4 hr specialized education, recreational and occupational therapy	sleepiness, somnolence, tachycardia, weight change, BMI change	
Shea et al., 2004 [76] **Country:** Canada **Condition category:** ASD **Funding:** Industry **Risk of bias:** Medium	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV	**Enrolled:** 80 **Analyzed:** 79 **Completed:** 72 **GROUP 1** **N:** 41 **Age, mean±SD (range):** 7.6±0 (5–12) **Males %:** 72.5 **Caucasian %:** NR **Diagnostic breakdown**	**Treatment duration:** 8 wk **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** anticholinergics, anticonvulsants and/or medications for sleep or anxiety (constant dose ≥30 days before enrolment), medications for preexisting organic disorders	**Benefits:** ABC, NCBRF, VAS-MS Response (ABC-I, CGI-C) **Harms:** Anorexia, behavioral issues, blood pressure, constipation, EPS (ESRS), fatigue, hyperkinesias, pulse,	In children with ASD, risperidone was well tolerated and efficacious in the treatment of autism associated behavioral symptoms.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
(subjective), Medium (objective)	**Inclusion criteria:** (1) physically healthy outpatients, (2) 5–12 yr, (3) DSM-IV Axis I dx of PDD, (4) a total score >30 on the CARS with or without MR **Exclusion criteria:** (1) patients with schizophrenia, other psychotic disorders, clinically relevant nonneurologic disease, clinically significant laboratory abnormalities, or a seizure disorder for which they were receiving >1 anticonvulsant or if they had had a seizure in the last 3 mo, (2) history of hypersensitivity to neuroleptics, tardive dyskinesia, NMS, drug or alcohol abuse, or HIV infection, (3) used risperidone in the last 3 mo or previously unresponsive or intolerant to risperidone, (4) using a prohibited medication	**(n):** Asperger's disorder (5), autistic disorder (27), childhood disintegrative disorder (1), PDD NOS (7), Rett disorder (0) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (15) **GROUP 2** **N:** 39 **Age, mean±SD (range):** 7.3±0 (5–12) **Males %:** 82.1 **Caucasian %:** NR **Diagnostic breakdown (n):** Asperger's disorder (7), autistic disorder (28), childhood disintegrative disorder (0), PDD NOS (4), Rett disorder (0) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (12)	**Prohibited drugs:** α-2 antagonists, antidepressants, antipsychotics, cholinesterase inhibitors, clonidine, guanfacine, lithium, naltrexone, psychostimulants **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.2 **Concurrent treatments:** analgesics (15), anti-asthmatics (6), antibiotics (5), anticholinergics (3), cough and cold preparations (10), sedatives/hypnotics (11) **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** analgesics (7), anti-asthmatics (4), antibiotics (5), anticholinergics (1), cough and cold preparations (4), sedatives/hypnotics (9)	SAE, somnolence, tachycardia, tardive dyskinesia, total AE, WAE, weight change	
Sikich et al., 2008[78] **Country:** USA	**Recruitment dates:** Feb 2002 to May 2006 **Study design:** RCT (parallel)	**Enrolled:**116 **Analyzed:** NR **Completed:** 70 **GROUP 1**	**Treatment duration:** 8 wk (10.1 mo extension) **Run-in phase:** Yes **Run-in phase duration:** 2 wk	**Benefits:** BPRS-C, CGI-I, CGI-S, CAFAS, PANSS, medication adherence, response,	Rispiridone and olanzapine failed to show superior efficacy over molindone in the

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Condition category: Schizophrenia and related **Funding:** Government **Risk of bias:** Low (subjective), Low (objective)	**Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV, KID-SCID **Inclusion criteria:** (1) 8–19 yr (30% or fewer 16 or older), (2) DSM-IV dx of schizophrenia, schizoaffective disorder, or schizophreniform disorder with current positive psychotic symptoms of at least moderate intensity, (PANSS or BRRS-C), (3) good physical health, (4) able to provide informed consent and guardian's written informed consent **Exclusion criteria:** (1) premorbid dx of MR, (2) current major depressive episode, active substance abuse, (3) history of intolerance or nonresponse to any of the study treatments during a prior episode, (4) history of successful use of the study treatments during the current episode (≥8 wk of treatment, including ≥2	**N:** 41 **Age, mean±SD (range):** NR **Males %:** 57.5 **Caucasian %:** 70 **Diagnostic breakdown (n):** schizoaffective disorder (14), schizophrenia (26) **Treatment naïve (n):** 16 **Inpatients (n):** 4 **First episode psychosis (n):** 35 **Comorbidities:** ADHD (12), affective disorder (9), anxiety disorder (6), ASD (2), DBD (4), learning disability (7), MR (0), none (14), psychosis (7), SA (4) **GROUP 2** **N:** 36 **Age, mean±SD (range):** NR **Males %:** 71.4 **Caucasian %:** 60 **Diagnostic breakdown (n):** schizoaffective disorder (13), schizophrenia (22) **Treatment naïve (n):** 13 **Inpatients (n):** 2 **First episode psychosis (n):** 33 **Comorbidities:** ADHD (13), affective disorder (7), anxiety disorder (9), ASD (2), DBD (6), learning disability (1), MR (0), none (17), psychosis (4), SA (2) **GROUP 3**	**Permitted drugs:** antidepressants or non-antipsychotic mood stabilizers (≥4 wk prior to study entry); anticholinergics, benzodiazepines, propranolol (concomitant); thymoleptics (maintenance phase) **Prohibited drugs:** NR **GROUP 1** **Drug name:** Molindone **Dosing variability:** variable **Target dose (mg/day):** 140 **Daily dose (mg/day), mean±SD (range):** 59.9±33.5 (10–140) **Concurrent treatments:** antidepressants (4), benzodiazepines (39%), mood stabilizers (3), propranolol (13%), benzotropine (45%) **GROUP 2** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** 20 **Daily dose (mg/day), mean±SD (range):** 11.4±5 (2.5–20) **Concurrent treatments:** antidepressants (4), benzodiazepines (20%), benztropine (14%), mood stabilizers (2), propranolol (11%) **GROUP 3** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** 6 **Daily dose (mg/day), mean±SD (range):** 2.8±1.4 (0.5–6) **Concurrent treatments:** antidepressants (5),	suicide **Harms:** Akathisia, behavioral issues, blood pressure, BMI, constipation, dystonia, ECG changes, SAS, BAS, AIMS, EPS, glucose, homeostasis, insulin, lipid profile, liver function, prolactin, prolactin-related AE, pulse, SAE, sedation, tardive dyskinesia, total AE, WAE, weight change	treatment of early-onset schizophrenia and schizoaffective disorder.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	wk at the maximal dose allowed in the current study), (5) imminent risk of harming themselves or others, (6) bipolar disorder, primary PTSD, primary personality disorder, or psychosis NOS (dx by clinician, confirmed by KID-SCID), (7) endocrinological or neurological conditions that confound the dx or are a contraindication to treatment, (8) pregnancy or refusal to practice contraception during the study, (9) use of a depot antipsychotic within the past 6 mo	**N:** 42 **Age, mean±SD (range):** NR **Males %:** 65.9 **Caucasian %:** 61 **Diagnostic breakdown (n):** schizoaffective disorder (13), schizophrenia (28) **Treatment naïve (n):** 9 **Inpatients (n):** 6 **First episode psychosis (n):** 40 **Comorbidities:** ADHD (9), affective disorder (12), anxiety disorder (12), ASD (3), DBD (10), learning disability (2), MR (0), none (15), psychosis (6), SA (2)	benzodiazepines (41%), benztropine (34%), mood stabilizers (4), propranolol (7%)		
Sikich et al., 2004 [77] **Country:** USA **Condition category:** Schizophrenia and related **Funding:** Industry, Government, Foundation **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** Nov 1997 to May 2001 **Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV, K-SADS-P **Inclusion criteria:** (1) ≥1 positive psychotic symptom of moderate or greater severity on the BPRS-C, present throughout the past 2 wk, (2) full scale IQ >69, (3) patients with	**Enrolled:** 50 **Analyzed:** 50 **Completed:** 32 **GROUP 1** **N:** 15 **Age, mean±SD (range):** 15.4±2.2 **Males %:** 53 **Caucasian %:** 73 **Diagnostic breakdown (n):** affective disorders (7), schizophrenia spectrum (8) **Treatment naïve (n):** 3 **Inpatients (n):** 10 **First episode psychosis (n):** 12	**Treatment duration:** 8 wk **Run-in phase:** Yes **Run-in phase duration:** 1–2 wk **Permitted drugs:** amantadine (200 mg/day), antidepressants and mood stabilizers (if taken ≥4 wk preceding study entry or if clinically significant affective symptoms persisted after 4 wk of study treatment), benztropine (1–3 mg/day), lorazepam (0.5–3 mg/day), propranolol (20–60 mg/day), trihexyphenidyl (4–6 mg/day) **Prohibited drugs:** NR **GROUP 1** **Drug name:** Haloperidol	**Benefits:** BPRS-C, CPRS, CGI-I, CGI-S, response, medication adherence **Harms:** Withdrawal due to AEs, akathisia, BMI, constipation, dermatolodic AE, dystonia, ECG changes, EPS, SAS, AIMS, tardive dyskinesias, glucose, lipid profile, prolactin, prolactin-related AE, sedation, WAE, weight changes, white blood cells	Risperidone and olanzapine were effective in acutely reducing symptoms in psychotic youth.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	current or recent dx of ADHD, Tourette syndrome, OCD, or a history of substance abuse or dependence were allowed to participate only if their psychotic symptoms were not better accounted for by the comorbid disorder **Exclusion criteria:** (1) psychotic symptoms resulting from acute substance intoxication or withdrawal, (2) history of serious adverse reactions or nonresponse to an adequate trial of any of the study medications during this psychotic episode, (3) prior dx of PDD or a serious medical or neurological disorder, (4) pregnancy or refusal to practice contraception, (5) imminent risk in current setting to harm self or others	**GROUP 2** **N:** 16 **Age, mean±SD (range):** 14.6±3.1 **Males %:** 56 **Caucasian %:** 63 **Diagnostic breakdown (n):** affective disorders (11), schizophrenia spectrum (5) **Treatment naïve (n):** 8 **Inpatients (n):** 12 **First episode psychosis (n):** 12 **GROUP 3** **N:** 19 **Age, mean±SD (range):** 14.6±2.9 **Males %:** 68 **Caucasian %:** 47 **Diagnostic breakdown (n):** affective disorders (6), schizophrenia spectrum (13) **Treatment naïve (n):** 2 **Inpatients (n):** 15 **First episode psychosis (n):** 15	**Dosing variability:** variable **Target dose (mg/day):** 1–5 **Daily dose (mg/day), mean±SD (range):** 5±2 (1–5) **Concurrent treatments:** amantadine (1), benztropine/trihexyphenidyl (7), buproprion (4), citalopram (1), gabapentin (1), lithium (1), lorazepam (3), paroxetine (1), sertraline (3), valproate (2), venlaflaxine (1), inpatient or residential treatment (9) **GROUP 2** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** 2.5–12.5 **Daily dose (mg/day), mean±SD (range):** 12.3±3.5 (2.5–12.5) **Concurrent treatments:** benztropine/trihexyphenidyl (5), buproprion (2), carbamazepine (1), fluoxetine (2), fluvoxamine (1), lithium (1), lorazepam (1), paroxetine (1), propranolol (2), sertraline (1), valproate (1), inpatient or residential treatment (10) **GROUP 3** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** 0.5–3 **Daily dose (mg/day), mean±SD (range):** 4±1.2 (0.5–3) **Concurrent treatments:** amantadine(2), benztropine/ trihexyphenidyl (4), citalopram (1), clomipramine (1), gabapentin with lamotrigine (1), lorazepam(2), propranolol (1), sertraline (2), trazadone (1), valproate (3),		

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
			inpatient or residential treatment (11)		
Singh, 2011 [79] **Country:** Russia, India, Ukraine, United States, Romania **Condition category:** Schizophrenia and related **Funding:** Industry **Risk of bias:** High (subjective), Medium (objective)	**Recruitment dates:** Jul 2007 to Mar 2009 **Study design:** RCT (parallel) **Setting:** Hospitalization permitted for first 3 wks **Diagnostic criteria:** DSM-IV, K-SADS-PL **Inclusion criteria:** (1) 12–17 yr, (2) body weight ≥29 kg, (3) DSM-IV criteria for schizophrenia ≥1 yr before screening and history of at least 1 antipsychotic, (4) PANSS total score 60–120 (acute symptomatic), (5) physically healthy based on medical history, physical examination, ECG, and laboratory test results **Exclusion criteria:** (1) dissociative disorder, BD, MDD, schizoaffective disorder, schizophreniform disorder, ASD, or primary substance induced psychotic disorder (DSM-IV), (2)	**Enrolled:** 201 **Analyzed:** 200 **Completed:** 139 **GROUP 1** **N:** 54 **Age, mean±SD (range):** 15.1±1.5 **Males %:** 56 **Caucasian %:** 65 **Treatment naïve (n):** 7 **Inpatients (n):** NR **First episode psychosis (n):** 0 **GROUP 2** **N:** 48 **Age, mean±SD (range):** 15.3±1.6 **Males %:** 65 **Caucasian %:** 71 **Treatment naïve (n):** 4 **Inpatients (n):** NR **First episode psychosis (n):** 0 **GROUP 3** **N:** 48 **Age, mean±SD (range):** 15.5±1.6 **Males %:** 70 **Caucasian %:** 68 **Treatment naïve (n):** 7 **Inpatients (n):** NR **First episode psychosis (n):** 0 **GROUP 4** **N:** 51 **Age, mean±SD (range):**	**Treatment duration:** 6 wk **Run-in phase:** Yes **Run-in phase duration:** ≤3 wk **Permitted drugs:** propranolol (for akathisia), antiparkinsonians (benzotropine, biperiden), lorazepam (rescue) **Prohibited drugs:** alcohol, antipsychotics, antidepressants, drugs of abuse, lithium, psychostimulants, anticonvulsants, sedatives, cholinesterase inhiitors **GROUP 1** **Drug name:** Paliperidone ER (low) **Dosing variability:** fixed **Target dose (mg/day):** 1.5 (all weights) **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** anti-EPS (2), benzodiazepines (13), propranolol (1) **GROUP 2** **Drug name:** Paliperidone ER (medium) **Dosing variability:** fixed **Target dose (mg/day):** 3 (<51 kg), 6 (≥51 kg) **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** anti-EPS (7), benzodiazepines (16), propranolol (1) **GROUP 3** **Drug name:** Paliperidone ER (high)	**Benefits:** CGAS, CGI-S, PANSS, VAS-sleep, response rate, suicide, medication adherence **Harms:** Blood pressure, ECG changes, QTcLD, orthostatic hypotension, NMS, tachycardia, glucose, insulin resistance, prolactin levels, mortality, NMS, serious AEs, seizure, total AE, WAE, weight change, glucose homeostasis, AIMS, SAS	The medium dose paliperidone ER group was statistically superior to the placebo group according to the primary efficacy analysis by weight-based, fixed-dose treatment group. When analyzed by actual dose group, all three doses of paliperidone showed improvement relative to placebo.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	mild, moderate, or severe MR, (3) pregnant, (4) known or suspected history of seizure disorder, NMS, encephalopathic syndrome, tardive dyskinesia, or insulin dependent diabetes mellitus, (5) presence of any significant or unstable systemic disease, (6) clozapine in 2 months before treatment	15.7±1.4 **Males %:** 55 **Caucasian %:** 69 **Treatment naïve (n):** 3 **Inpatients (n):** NR **First episode psychosis (n):** 0	**Dosing variability:** fixed **Target dose (mg/day):** 6 (<51 kg), 12 (≥51 kg **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** anti-EPS (14), benzodiazepines (15), propranolol (1) **GROUP 4** **Drug name:** Placebo **Dosing variability:** fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** anti-EPS (0), benzodiazepines (19), propranolol (0)		
Snyder et al., 2002 [80] **Country:** Canada, South Africa, USA **Condition category:** ADHD **Funding:** Foundation **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV, VABS **Inclusion criteria:** (1) CD, ODD, or DBD-NOS (DSM-IV), (2) parent/ caregiver rating ≥24 on the Conduct Problem subscale of the NCBRF, (3) IQ 36–84 inclusive, (4) VABS score ≤84, (5) healthy on the basis of a pretrial physical examination, medical	**Enrolled:** 110 **Analyzed:** 110 **Completed:** 85 **GROUP 1** **N:** 53 **Age, mean±SD (range):** 8.6±0.3 (5–12) **Males %:** 77.4% **Caucasian %:** 78.8% **Diagnostic breakdown (n):** CD (3), CD/ADHD (16), Combined/No ADHD (9), ODD/ DBD (6), ODD/DBD/ADHD (28) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (44) **GROUP 2** **N:** 57	**Treatment duration:** 6 wk **Run-in phase:** Yes **Run-in phase duration:** 1 wk **Permitted drugs:** stable doses (≥30 days prior to study) of anticholinergics, antihistamines, chloral hydrate, medication for preexisting medical conditions, melatonin, psychostimulants (comorbid ADHD) **Prohibited drugs:** no other medication permitted **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1±0.1 SE (0.4–3.8) **Concurrent treatments:** NR **GROUP 2**	**Benefits:** ABC, BPI, CGI-I, CGI-S, NCBRF, VAS Medication adherence **Harms:** Anorexia, behavioral issues, Bucco-linguo-masticatory score, BMI, ECG changes, EPS, fatigue, parkinsonism, prolactin, prolactin-related AE, pulse, SAE, somnolence, tardive dyskinesia, total AE, WAE, weight change	Risperidone was adequately tolerated and was effective in treating children with subaverage IQs and severe disruptive behaviors.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	history, and ECG, (6) consent by parent/ caregiver, (7) 5–12 yr **Exclusion criteria:** (1) PDD, schizophrenia, or other psychotic disorders, (2) head injury as a cause of impaired IQ, (3) seizure condition requiring medication, (4) females who were sexually active without a reliable form of birth control, (5) serious or progressive illness or clinically abnormal laboratory values, (6) history of tardive dyskinesia, NMS, or hypersensitivity to any antipsychotic drug, (7) known presence of HIV, (8) previous treatment with risperidone	**Age, mean±SD (range):** 8.8±0.3 (5–12) **Males %:** 73.7% **Caucasian %:** 73.7% **Diagnostic breakdown (n):** CD (7), CD/ADHD (15), Combined/No ADHD (17), ODD/ DBD (10), ODD/DBD/ADHD (25) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (40)	**Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR		
Spencer et al., 1994 [81] **Country:** USA **Condition category:** Schizophrenia and related **Funding:** Industry, Government **Risk of bias:** Medium	**Recruitment dates:** Sep 1989 to May 1991 **Study design:** RCT (crossover) **Setting:** Inpatient **Diagnostic criteria:** DSM-III-TR, DICA-R **Inclusion criteria:** (1) actively psychotic prepubertal patients, (2) 5–11 yr, (3)	**Enrolled:** 16 **Analyzed:** 16 **Completed:** 16 **GROUP 1** **N:** 16 (crossover) **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR	**Treatment duration:** 8 wk **Run-in phase:** Yes **Run-in phase duration:** 2 wk **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Haloperidol **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 2 (0.5–3.5) **Concurrent treatments:** NR	**Benefits:** BPRS-C, CGI-I, CGI-S, CPRS **Harms:** Drowsiness, dystonia	Haloperidol improved the target psychotic symptoms in children with schizophrenia.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
(subjective), Medium (objective)	admitted to the Bellevue Hospital Children's Inpatient Psychiatric Unit, (4) schizophrenia **Exclusion criteria:** (1) intercurrent systemic illness, (2) seizure disorder, (3) MR below borderline, (4) tardive dyskinesia, (5) infantile autism, (6) receipt of psychoactive medication within 4 wk of double-blind treatment	**GROUP 2** **N:** 16 (crossover) **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR	**GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 2.5±0.5 (0.5–3.5) **Concurrent treatments:** NR		
Stocks et al., 2012 [82] **Country:** USA **Condition category:** ADHD **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** October 2008 – September 2009 **Study design:** RCT (parallel) **Setting:** outpatient **Diagnostic criteria:** K-SADS-PL, DSM-IV-TR **Inclusion criteria:** 6-12 yr, ADHD with persistent serious conduct problems (≥27 on DBD, ≥2 on Conduct problem subscale of NCBRF-TIQ for: knowingly destroys property, gets in physical fights, physically attacks people. Weigh ≥ 16kg,	**Enrolled:** 78 **Analyzed:** 78 **Completed:** 55 **GROUP 1** **N:** 20 **Age, mean±SD (range):** 8.5±1.88 yr **Males %:** 95% **Caucasian %:** 55% **Diagnostic breakdown (n):** ADHD (20) **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** 0 **Comorbidities (n):** Asthma (5), CD (2), Enuresis (4), Insomnia (1), ODD (6), Seasonal allergies (2) **GROUP 2** **N:** 19 **Age, mean±SD (range):**	**Treatment duration:** 8-11 wk (2-5 wk titration, 6 wk maintenance) **Run-in phase:** Yes **Run-in phase duration:** 2 wk **Permitted drugs:** methylphenidate, amphetamine, benzotropine **Prohibited drugs:** other antipsychotics, antidepressants, hypnotics, anticonvulsants, antihypertensives, antihistamines **GROUP 1** **Drug name:** Molindone hydrochloride **Dosing variability:** Fixed **Target dose (mg/day):** <30 kg: 5 mg/day; ≥ 30 kg: 10 mg/day **Daily dose (mg/day), mean±SD (range):** <30 kg: 5 mg/day; ≥ 30 kg: 10 mg/day **Concurrent treatments:** Stable dose of FDA approved psychostimulant (methylphenidate	**Benefits:** NCBRF-TIQ, CGI-I, CGI-S, SNAP-IV **Harms:** Somnolence, metabolic effects, neuromotor effects, infection, prolactin related events	Molindone showed clinical benefit with an acceptable side-effect profile in this study. Preliminary efficacy results suggest that molindone produces dose-related behavioral improvements over 9-12 weeks.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	IQ ≥ 71, free of antipsychotics for at least 2 weeks pre-baseline, receiving stable dose of an FDA approved psychostimulant for at least 30 days pre-baseline, otherwise in good physical health **Exclusion criteria:** Current or lifetime diagnosis of BP, PTSD, personality disorder, psychotic disorder, currently meeting diagnostic criteria for major depressive disorder, OCD, PDD or other AD as primary disorder	9.4±1.98 yr **Males %:** 84.2% **Caucasian %:** 57.9% **Diagnostic breakdown (n):** ADHD (19) **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** 0 **Comorbidities (n):** Asthma (3), CD (2), Eczema (3), Enuresis (3), Environmental allergies (1), Insomnia (2), ODD (7), Seasonal allergies (1) **GROUP 3** **N:** 19 **Age, mean±SD (range):** 8.8±2.12 yr **Males %:** 68.4% **Caucasian %:** 42.1% **Diagnostic breakdown (n):** ADHD (19) **Treatment naïve (n):** **Inpatients (n):** **First episode psychosis (n):** 0 **Comorbidities (n):** Asthma (4), CD (3), Eczema (2), Enuresis (2), Environmental allergies (1), ODD (6) **GROUP 4** **N:** 20 **Age, mean±SD (range):** 8.8±2.00 yr **Males %:** 95% **Caucasian %:** 65% **Diagnostic breakdown (n):** ADHD (20)	or amphetamine) **GROUP 2** **Drug name:** Molindone hydrochloride **Dosing variability:** Fixed **Target dose (mg/day):** <30 kg: 10 mg/day; ≥ 30 kg: 20 mg/day **Daily dose (mg/day), mean±SD (range):** <30 kg: 10 mg/day; ≥ 30 kg: 20 mg/day **Concurrent treatments:** Stable dose of FDA approved psychostimulant (methylphenidate or amphetamine) **GROUP 3** **Drug name:** Molindone hydrochloride **Dosing variability:** Fixed **Target dose (mg/day):** <30 kg: 15 mg/day; ≥ 30 kg: 30 mg/day **Daily dose (mg/day), mean±SD (range):** <30 kg: 15 mg/day; ≥ 30 kg: 30 mg/day **Concurrent treatments:** Stable dose of FDA approved psychostimulant (methylphenidate or amphetamine) **GROUP 4** **Drug name:** Molindone hydrochloride **Dosing variability:** Fixed **Target dose (mg/day):** <30 kg: 20 mg/day; ≥ 30 kg: 40 mg/day **Daily dose (mg/day), mean±SD (range):** <30 kg: 20 mg/day; ≥ 30 kg: 40 mg/day **Concurrent treatments:** Stable dose of FDA approved psychostimulant (methylphenidate		

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Treatment naïve (n): NR **Inpatients (n):** 0 **First episode psychosis (n):** 0 **Comorbidities (n):** Asthma (1), CD (1), Eczema (1), Enuresis (3), Environmental allergies (2), Insomnia (2), ODD (7), Seasonal allergies (2)	or amphetamine)		
Swadi et al., 2010 [83] **Country:** New Zealand **Condition category:** Schizophrenia and related **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Inpatient **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) <19 yr, (2) first obset psychotic disorder or a mood disorder with psychotic features **Exclusion criteria:** (1) alcohol or substance dependence not in full remission, (2) prior treatment with atypical antipsychotic drugs	**Enrolled:** 22 **Analyzed:** 22 **Completed:** 22 **GROUP 1** **N:** 11 **Age, mean±SD (range):** NR **Males %:** 54.5 **Caucasian %:** NR **Treatment naïve (n):** 11 **Inpatients (n):** all **First episode psychosis (n):** 11 **Comorbidties**: SUD (0) **GROUP 2** **N:** 11 **Age, mean±SD (range):** NR **Males %:** 63.6 **Caucasian %:** NR **Treatment naïve (n):** 11 **Inpatients (n):** all **First episode psychosis (n):** 11 **Comorbidties**: SUD (0)	**Treatment duration:** 6 wk **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 607 (100–800) **Concurrent treatments:** anticholinergics (1), cognitive behavioral therapy, family work, activity-based interventions allowed **GROUP 2** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 2.9 (1.5–5) **Concurrent treatments:** anticholinergics (5), cognitive behavioral therapy, family work, activity-based interventions allowed	**Benefits:** BPRS, PANSS, response (BPRS, CGI-S, HAM-D, PANSS, YMRS) **Harms:** Blood pressure, SAS, BAS, AIMS, glucose, lipid profile, liver function, prolactin, sedation, weight change	Risperidone may be more beneficial than quetiapine for adolescent patients with bipolar disorder.
Tohen et al., 2007 [84]	**Recruitment dates:** Nov 2002 to May 2005	**Enrolled:** 161 **Analyzed:** 161 **Completed:** 120	**Treatment duration:** 3 wk **Run-in phase:** Yes **Run-in phase duration:** 2–14 day	**Benefits:** CDRS, CGI-BP (overall, mania, depression	Olanzapine was more effective in treating adolescents

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Country: Puerto Rico, USA **Condition category:** Bipolar disorder **Funding:** Industry **Risk of bias:** Medium (subjective), Medium (objective)	**Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV-TR, K-SADS-PL **Inclusion criteria:** (1) 12–17 yr, (2) manic or mixed bipolar episodes (with or without psychotic features), (3) inpatient or outpatient, (4) total score ≥20 on the Adolescent Structured YMRS **Exclusion criteria:** (1) prior nonreponse to olanzapine, (2) treatment within the previous 30 day with an experimental medication not available for clinical use, (3) suicide risk, (4) clinically significant abnormal laboratory values at baseline, (5) DSM-IV-TR substance dependence (excluding nicotine and caffeine) within the last 30 days, (6) treatment with long-lasting neuroleptic within 14 day prior to randomization	**GROUP 1** **N:** 107 **Age, mean±SD (range):** 15.1±1.3 **Males %:** 57 **Caucasian %:** 66.4 **Diagnostic breakdown (n):** mixed (61), psychotic features (22), rapid cycling (25) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (45), DBD (37) **GROUP 2** **N:** 54 **Age, mean±SD (range):** 15.4±1.2 **Males %:** 44.4 **Caucasian %:** 75.9 **Diagnostic breakdown (n):** mixed (25), psychotic features (7), rapid cycling (5) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (13), DBD (12)	**Permitted drugs:** anticholinergics (2–6mg/day), benzodiazepines/hypnotics (≤2 mg/day lorazepam equivalents for ≤3 consecutive days), psychostimulants (constant dose ≥30 day prior to randomization and through study) **Prohibited drugs:** anticholinergics **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 8.9 (2.5–20) **Concurrent treatments:** anticholinergics (4.7%), benzodiazepines (12.1%) **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** anticholinergic medication (0), benzodiazepines (7.4%)	subscales), ADHS IV, OAS, YMRS (total+item analysis), HRQoL(subscales); Olsen 2012, response, suicide **Harms:** Bipolar exacerbation, blood cells, blood pressure, BMI, ECG changes, EPS (AIMS, BAS, SAS), glucose, hepatic enzyme, lipid profile, mortality, prolactin, prolactin-related AE, pulse, SAE, weight change	with bipolar mania and placebo; however, it resulted in significantly greater weight gain.
Tramontina et al., 2009 [85]	**Recruitment dates:** Jan 2005 to Nov 2007	**Enrolled:** 43 **Analyzed:** 43	**Treatment duration:** 6 wk **Run-in phase:** No	**Benefits:** CDRS, CGI-S, CMRS-P,	Aripiprazole was effective in

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Completed: 41	**Run-in phase duration:** NR	YMRS, medication adherence, response, suicide	decreasing mania symptoms and improving global functioning without resulting in severe advserse events or weight gain.
Country: Brazil **Condition category:** Bipolar disorder **Funding:** Industry, Government, Hospital **Risk of bias:** Low (subjective), Low (objective)	**Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV, K-SADS-E **Inclusion criteria:** (1) 8–17 yr, (2) DSM IV bipolar I or II disorder comorbid with ADHD, (3) clear reports of ADHD symptom onset preceding any mood symptomology, (4) acutely manic or mixed states (YMRS score ≥20 at baseline visit) **Exclusion criteria:** (1) estimated IQ < 70 (WISC-III), (2) use of any medication 4 wk prior to entering the study, (3) dx of PDD, schizophrenia, or substance abuse or dependence, (4) severe suicide/homicide risk, (5) previous use of aripiprazole, (6) other acute or chronic diseases, (7) pregnancy	**GROUP 1** **N:** 18 **Age, mean±SD (range):** 11.7±2.7 **Males %:** 33 **Caucasian %:** 83 **Treatment naïve (n):** ND **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** ADHD (all), anxiety disorders (8), DBD (15), psychosis (8), SA (0) **GROUP 2** **N:** 25 **Age, mean±SD (range):** 12.2±2.8 **Males %:** 56 **Caucasian %:** 96 **Treatment naïve (n):** ND **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** ADHD (all), anxiety disorders (13), DBD (20), psychosis (8), SA (0)	**Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Aripiprazole **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 13.6±5.4 (5–20) **Concurrent treatments:** none **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 15±3.2 (10–20) **Concurrent treatments:** none	**Harms:** Akathisia, behavioral issues, dermatologic AE, dyskinesia, EPS, fatigue, seizure, somnolence, weight change	
Troost et al., 2005 [86] **Country:**	**Recruitment dates:** NR **Study design:** RCT	**Enrolled:** 24 **Analyzed:** 24 **Completed:** NR	**Treatment duration:** 6 mo **Run-in phase:** Yes **Run-in phase duration:** 1–4 wk	**Benefits:** ABC (sub scores), CGI, VAB, cognitive (focused and divided attention	Risperidone was effective in reducing disruptive behavior in about half of

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Netherlands **Condition category:** ASD **Funding:** Industry, Foundation **Risk of bias:** Low (subjective), Low (objective)	(parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV-TR, ADI-R **Inclusion criteria:** (1) DSM-IV-TR criteria for PDD, (2) demonstrated clinically significant tantrums, aggression, self-injurious behavior, or a combination of these, (3) 5–17 yr, (4) weight ≥15 kg, (5) mental age ≥18 mo **Exclusion criteria:** (1) children on effective psychotropic drug treatment for disruptive behavior	**GROUP 1** **N:** 12 **Age, mean±SD (range):** 9.4±3.4 **Males %:** 91.6 **Caucasian %:** 100 **Diagnostic breakdown (n):** Asperger's disorder (1), autistic disorder (3), PDD NOS (8) **Treatment naïve (n):** 11 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (2) **GROUP 2** **N:** 12 **Age, mean±SD (range):** 8.7±1.2 **Males %:** 91.6 **Caucasian %:** 83 **Diagnostic breakdown (n):** Asperger's disorder (1), autistic disorder (3), PDD NOS (8) **Treatment naïve (n):** all **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (0)	**Permitted drugs:** anticonvulsants (stable dose for ≥4 wk and patient seizure-free for ≥6 mo), stimulants (comorbid ADHD) **Prohibited drugs:** psychotropics **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.9±0.7 **Concurrent treatments:** stimulants (1), stimulant and anticonvulsant (1) **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.7±0.5 **Concurrent treatments:** stimulants (2)	task), response (relapse) **Harms:** Dyskinesia (SAS, AIMS)	children with ASD.
Van Bellinghen et al., 2001 [87] **Country:** Belgium **Condition category:** Behavioral issues **Funding:** Industry	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Inpatient **Diagnostic criteria:** clinical assessment and parent interview	**Enrolled:** 13 **Analyzed:** 13 **Completed:** 13 **GROUP 1** **N:** 6 **Age, mean±SD (range):** NR (6–14) **Males %:** 33.3 **Caucasian %:** NR **Treatment naïve (n):** NR	**Treatment duration:** 4 wk **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** antiepileptics **Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable	**Benefits:** ABC, CGI-I, PAC, VAS **Harms:** Parkinsonism, pulse, somnolence, total AE, weight change, EP disorder (ESRS)	Risperidone was well tolerated, and there was no difference between risperidone- and placebo-treated groups with respect to the occurrence of extrapyramidal side effects.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Risk of bias: Medium (subjective), Medium (objective)	**Inclusion criteria:** (1) 6–18 yr, (2) IQ 45–85, (3) demonstrating persistent behavioral disturbances **Exclusion criteria:** (1) presence of a clinically relevant non-neurologic disease, (2) abnormal laboratory tests, (3) epileptic crisis in the previous 3 mo, (4) participation in a drug trial in the previous 4 wk, (5) remoxipride treatment in the previous 4 wk, (6) oral neuroleptics and other psychotropics in the previous wk, (6) previous treatment with remoxipride combined with abnormal hematologic values, (7) a depot neuroleptic injection within one treatment cycle of the time of selection, (8) female patients of reproductive age if their contraceptive use was considered inadequate, (9) pregnant or lactating	**Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** anxiety (0), depression (0), mania (0), MR (all) **GROUP 2** **N:** 7 **Age, mean±SD (range):** NR (7–14) **Males %:** 42.9 **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** anxiety (0), depression (0), mania (0), MR (all)	**Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.2 **Concurrent treatments:** valproate (1) **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR		
Van Bruggen et al., 2003 [88] **Country:** Netherlands	**Recruitment dates:** NR **Study design:** RCT (parallel)	**Enrolled:** 44 **Analyzed:** 42 **Completed:** NR **GROUP 1**	**Treatment duration:** Olanzapine 9.8 wk, Risperidone 6.7 wk **Run-in phase:** No **Run-in phase duration:** NA	**Benefits:** PANSS, medication adherence, response **Harms:** BAS, SAS,	Symptom response was similar in the olanzapine and risperidone groups.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Condition category: Schizophrenia and related **Funding:** Industry, Government **Risk of bias:** High (subjective), High (objective)	**Setting:** Inpatient **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) 16–28 yr, (2) first or second psychotic episode according to DSM-IV criteria of schizophrenia, schizofreniform or schizoaffective disorder, (3) actively symptomatic at study entry (PANSS score of moderate or higher on items for delusions, conceptual disorganization, or hallucinations) **Exclusion criteria:** (1) epilepsy, (2) toxic psychosis or infectious disorder, (3) a primary dx of substance abuse (drugs or alcohol), (4) MR, (5) pregnant or lactating female patients, (6) concomitant use of other antipsychotic agents, (7) treatment with an injectable depot neuroleptic less than one dosing interval before study entry, (8) narrow-angle glaucoma and known hypersensitivity to	**N:** 18 **Age, mean±SD (range):** 21.0±2.8 **Males %:** 72 **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** 16 **GROUP 2** **N:** 26 **Age, mean±SD (range):** 20.6±3.0 **Males %:** 85 **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** 22	**Permitted drugs:** NR **Prohibited drugs:** antipsychotics **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 15.6±4 (5–30) **Concurrent treatments:** anticholinergics (2), antidepressants (0), benzodiazepines (7), mood stabilizers (0) **GROUP 2** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 4.4±1.5 (1–8) **Concurrent treatments:** anticholinergics (7), antidepressants (4), benzodiazepines (8), mood stabilizers (0)	AIMS, akathisia, parkinsonism, prolactin, prolactin-related AE, sedation, seizure, sexual dysfunction, somnolence, tachycardia, tardive dyskinesia, weight change	

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	olanzapine or risperidone, (9) insufficient knowledge of the Dutch language				
Weisler et al., 2011 [128] **Country:** USA **Condition category:** Depression **Funding:** Industry **Newcastle-Ottawa Scale:** 6/8 stars	**Recruitment Dates:** NR **Study design:** Observational (pooled analysis of 2 trials) **Diagnostic criteria:** DSM-IV-TR **Setting:** outpatients **Inclusion criteria:** Outpatients 18-65 yr (only looking at subgroup ≤ 25 yr here), major depressive episode ≥ 8 wk, inadequate response to ≥ 1 historical antidepressant **Exclusion criteria:** Significant risk of committing suicide during course of trial	**Enrolled:** 35 **Analyzed:** 35 **Completed:** 35 **GROUP 1:** **N:** 16 **Age, mean±SD (range):** ≤ 25 yr **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** 0 **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities (n):** NR **GROUP 2:** **N:** 19 **Age, mean±SD (range):** ≤ 25 yr **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** 0 **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities (n):** NR	**Treatment duration:** 6 wk **Run-in phase:** No **Run-in phase duration:** NA **Permitted drugs:** Escitalopram, fluoxetine, paroxetine CR, sertraline, venlafaxine XR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Aripiprazole **Dosing variability:** Variable **Target dose (mg/day):** 15 mg/day (paroxetine or fluoxetine) or 20 mg/day (all other patients) **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** Escitalopram, fluoxetine, paroxetine CR, sertraline, venlafaxine XR **GROUP 2:** **Drug name:** Placebo **Dosing variability:** Variable **Target dose (mg/day):** NA **Daily dose (mg/day), mean±SD (range):** NA **Concurrent treatments:** Escitalopram, fluoxetine, paroxetine CR, sertraline, venlafaxine XR	**Benefits:** suicide-related events and ideation **Harms:** NR	Adjunctive aripiprazole treatment represents a generally safe and relatively well-tolerated and efficacious treatment option for patients with MDD who had had an inadequate response to standard antidepressant medication.
Wink et al., 2014 [129] **Country:** USA **Condition**	**Recruitment dates:** July 2004 to Apr 2012 **Study design:** Retrospective	**Enrolled:** 142 **Analyzed:** 142 **Completed:** NR **GROUP 1** **N:** 72	**Treatment duration:** Risperidone (2.37±2.55 yr), Aripiprazole (1.47±1.21 yr) **Run–in phase:** NR **Run–in phase duration:** NR	**Benefits:** CGI-I **Harms:** Weight change (BMI, BMI-z)	Our results warrant further investigation using a prospective random assignment study design. Greater control of

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
category: ASD **Funding:** Industry/ non-industry **Newcastle-Ottawa Scale:** 7/8 stars	**Setting:** NR **Diagnostic criteria:** DSM-IV-TR **Inclusion criteria:** (1) 2-20 yr,(2) meets DSM-IV-TR criteria for ASD diagnosis, (3) subjects treated at the Christian Sarkine Autism Treatment Center (CSATC) **Exclusion criteria:** (1) Risperidone or aripiprazole use initiated prior to evaluation at CSATC, (2) individual received multiple antipsychotics at any time during treatment, (3) if <2 BMI data points were available	**Age, mean±SD (range):** 8.41±3.59yr **Males %:** 83.3 **Caucasian %:** 77.8 **Diagnostic breakdown (n):** Autistic disorder (40), PDD-NOS (29), Asperger's disorder (3) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** intellectual disability (34) **GROUP 2** **N:** 70 **Age, mean±SD (range):** 9.74±3.46yr **Males %:** 80 **Caucasian %:** 75.7 **Diagnostic breakdown (n):** Autistic disorder (44), PDD-NOS (19), Asperger's disorder (7) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** intellectual disability (30)	**Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 2.23±1.30 **Concurrent treatments:** SSRI (20), antiepileptic (5), stimulant (15), metformin (4), α 2-agonist (27), other (26) **GROUP 2** **Drug name:** Aripiprazole **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 11.85±7.23 **Concurrent treatments:** SSRI (21), antiepileptic (4), stimulant (10), metformin (2), α 2-agonist (22), benzodiazepine (2), other (24)		baseline characteristics, tracking detailed historical and lifestyle factors, use of methodical dosing guidelines, and limiting treatment duration may impact the results of such a study.
Wonodi et al., 2007 [130] **Country:** USA **Condition category:** Mixed conditions **Funding:** Non-	**Recruitment dates:** NR **Study design:** Retrospective **Setting:** Inpatient/ outpatient **Diagnostic criteria:**	**Enrolled:** 424 **Analyzed:** 198 **Completed:** 198 **GROUP 1** **N:** 118 **Age, mean±SD (range):** 11.9±2.8 yr **Males %:** 77.1 **Caucasian %:** 44.1	**Treatment duration:** ≥6mo **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Antipsychotic	**Benefits:** NR **Harms:** Tardive dyskinesia	Identifying the risk profiles of antipsychotic treatment in children would improve treatment outcomes in this vulnerable clinical population. Side-effect profile of the atypical

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
industry **Newcastle-Ottawa Scale:** 8/8 stars	NR **Inclusion criteria:** All children (5-18 yr) already receiving or likely to be prescribed antipsychotic medications at the referring facilities **Exclusion criteria:** NR	**Diagnostic breakdown (n):** Mood disorder NOS (103), ADHD (75) **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 80 **Age, mean±SD (range):** 10.7±3.9 yr **Males %:** 72.5 **Caucasian %:** 28.8 **Diagnostic breakdown (n):** Mood disorder NOS (67), ADHD (48) **Treatment naïve (n):** 80 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR	treatment ≥ 6mo **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** Anti-depressants (88), mood stabilizers (88), psychostimulants (80) **GROUP 2** **Drug name:** Antipsychotic naïve **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** Anti-depressants (38), mood stabilizers (22), psychostimulants (37)		antipsychotic drugs in children may be much different than in adults, underscoring the importance of risk-benefit discussions with patient families before treatment initiation, and ongoing monitoring for motor and other (e.g., metabolic) adverse events.
Woods et al., 2003 [89] **Country:** Canada, USA **Condition category:** Schizophrenia and related **Funding:** Industry, Government **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** Jan 1998 to July 2001 **Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV, COPS, Presence of Psychosis Scale **Inclusion criteria:** (1) help-seeking persons responding to advertisements or refered by clinicians,	**Enrolled:** 60 **Analyzed:** 59 **Completed:** 41 **GROUP 1** **N:** 31 **Age, mean±SD (range):** 18.2±5.5 **Males %:** 67.7 **Caucasian %:** 74.2 **Treatment naïve (n):** 28 **Inpatients (n):** NR **First episode psychosis (n):** all **Comorbidities:** SA (18) **GROUP 2** **N:** 29 **Age, mean±SD (range):**	**Treatment duration:** 1 yr **Run-in phase:** Yes **Run-in phase duration:** 3–14 day **Permitted drugs:** antidepressants, benztropine mesylate or biperiden (≤6 mg/day), chloral hydrate (max 1000 mg/day), diazepam (max 40 mg/day), lorazepam (max 8 mg/day), nizatidine (300–600 mg/day), propranalol hydrochloride **Prohibited drugs:** psychoactive medications **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** variable fixed at 5-15 mg/d	**Benefits:** SOPS, CGI-S, GAF, PANSS, MARDS, YMRS, cognitive (neurocognitive measures), medication adherence, response/conversion to psychosis **Harms:** Behavioral issues, blood pressure, EPS (AIMS, Barnes, ASA), glucose, fatigue, lipid profile, pulse, somnolence, WAE, weight change	The conversion-to-psychosis rate was not significantly different between treatment groups; however, olanzapine might reduce the conversion rate and delay onset of psychosis. Compared to placebo, olanzapine was efficacious for positive prodromal symptoms but induced weight gain.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	(2) 12–45 yr, (3) prodromal syndromes criteria using the Structured Interview for Prodromal Syndromes, (4) ability to understand and communicate with investigator, (5) informed consent/assent **Exclusion criteria:** (1) past or current DSM-IV psychotic disorder, (2) treatable psychiatric disorder that could account for prodromal symptoms, (3) suicidal or homicidal, (4) prodromal symptoms primarily sequelae of alcohol or drug use, (5) IQ <80, (6) seizure disorder without a clear or resolved etiology, (7) pregant or lactating, (8) took nonprotocol psychotropic medications	17.2±4 **Males %:** 62.1 **Caucasian %:** 58.6 **Treatment naïve (n):** 26 **Inpatients (n):** NR **First episode psychosis (n):** all **Comorbidities:** SA (9)	**Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 8±3.1 (5–15) **Concurrent treatments:** anticholinergics (1), benzodiazepines (7), nizatidine (1) **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 9.3±2.8 (5–15) **Concurrent treatments:** anticholinergics (2), benzodiazepines (2)		
Wudarsky et al., 1999 [131] **Country:** USA **Condition category:** Schizophrenia and related **Funding:** NR	**Recruitment dates:** NR **Study design:** Prospective cohort **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV, DSM-III-TR, structured interviews	**Enrolled:** 47 **Analyzed:** 47 **Completed:** NR **GROUP 1** **N:** 15 **Age, mean±SD (range):** 13.7±1.5 **Males %:** 60 **Caucasian %:** NR **Treatment naïve (n):** 0 **Inpatients (n):** NR	**Treatment duration:** 6 wk **Run-in phase:** Yes **Run-in phase duration:** 3 wk **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Haloperidol **Dosing variability:** variable **Target dose (mg/day):** NR	**Benefits:** NR **Harms:** Prolactin	Mean prolactin levels were significantly elevated after 6 weeks of treatment with haloperidol, clozapine, and olanzapine in patients with childhood-onset schizophrenia.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Newcastle-Ottawa Scale: 7/8 stars	**Inclusion criteria:** (1) DSM dx of schizophrenia, (2) resistant to treatment with two different FGAs **Exclusion criteria:** (1) onset of symptoms at ≥13 yr, (2) neurological or medical disease, (3) premorbid IQ <70	**First episode psychosis (n):** 0 **GROUP 2** **N:** 22 **Age, mean±SD (range):** 14.7±2.3 **Males %:** 72.7 **Caucasian %:** NR **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** 0 **GROUP 3** **N:** 10 **Age, mean±SD (range):** 14.2±2.9 **Males %:** 70 **Caucasian %:** NR **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** 0	**Daily dose (mg/day), mean±SD (range):** 15.3±8.2 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Clozapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 325.4±211 **Concurrent treatments:** NR **GROUP 3** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 17±3.5 **Concurrent treatments:** NR		
Yen et al., 2004 [90] **Country:** Taiwan **Condition category:** Schizophrenia and related **Funding:** Hospital **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** NR **Diagnostic criteria:** DSM-III-TR **Inclusion criteria:** (1) 18–65 yr, (2) total score >60 on PANSS **Exclusion criteria:** (1) psychoses other than schizophrenia, (2)	**Enrolled:** 8 **Analyzed:** 8 **Completed:** 8 **GROUP 1** **N:** 2 (≤24 yr) **Age, mean±SD (range):** 24.0 (24) **Males %:** 0 **Caucasian %:** NR **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 2** **N:** 6 (≤24 yr) **Age, mean±SD (range):**	**Treatment duration:** 2.8 mo **Run-in phase:** Yes **Run-in phase duration:** 1–4 wk **Permitted drugs:** biperiden or trihexylphenidyl; lorazepam, oxazepam or temazepam **Prohibited drugs:** NR **GROUP 1** **Drug name:** Haloperidol **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 11.2±6.9 (2–25) **Concurrent treatments:** NR	**Benefits:** PANSS **Harms:** NR	Risperidone was superior to haloperidol in improving negative symptoms and better tolerated during the treatment of schizophrenia.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	early childhood brain damage, (3) unable to comply with the medication, (4) severe illness, (5) pregnant or lactating women	20.7 (20–22) **Males %:** 66.7 **Caucasian %:** NR **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NR	**GROUP 2** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 4.4±2.6 (1–8) **Concurrent treatments:** NR		
Yoo et al., 2013 [92] **Country:** South Korea **Condition category:** Tic disorders **Funding:** Industry **Risk of Bias:** High (subjective), High (objective)	**Recruitment Dates:** August 2008 – April 2010 **Study design:** RCT (parallel) **Diagnostic criteria:** DSM-IV **Setting:** Outpatient clinics **Inclusion criteria:** 6-18 yr, DSM-IV diagnosis of Tourette syndrome or chronic motor or vocal tic disorder. Baseline total tic score ≥22 on YGTSS **Exclusion criteria:** Current mood disorders, schizophrenia and other psychotic disorders, or other psychiatric comorbidity requiring medication during study period, history of psychotropic substance or alcohol use disorders during 3 months pre-screening.	**Enrolled:** 61 **Analyzed:** 61 **Completed:** 54 **GROUP 1:** **N:** 32 **Age, mean±SD (range):** 11±2.5 yr **Males %:** 93.8% **Caucasian %:** NR **Diagnostic breakdown (n):** Tourette syndrome (32) **Treatment naïve (n):** NR **Inpatients (n):** (0) **First episode psychosis (n):** NR **Comorbidities (n):** ADHD (5), ODD (3), AD (0) **GROUP 2:** **N:** 29 **Age, mean±SD (range):** 10.9±3.0 yr **Males %:** 79.3% **Caucasian %:** NR **Diagnostic breakdown (n):** Tourette syndrome (29) **Treatment naïve (n):** NR **Inpatients (n):** (0) **First episode psychosis (n):** NR **Comorbidities (n):** ADHD (1), ODD (0), AD (1)	**Treatment duration:** 10 wk **Run-in phase:** Yes **Run-in phase duration:** Free of antipsychotic or antiparkinson drugs 1 wk before randomization, free of fluoxetine 4 wk before **Permitted drugs:** Aripiprazole (for group 1) **Prohibited drugs:** All other drugs **GROUP 1** **Drug name:** Aripiprazole **Dosing variability:** Fixed **Target dose (mg/day):** 20 mg/day **Daily dose (mg/day), mean±SD (range):** 11.0±6.1 mg/day **Concurrent treatments:** NR **GROUP 2:** **Drug name:** Placebo **Dosing variability:** Fixed **Target dose (mg/day):** NA **Daily dose (mg/day), mean±SD (range):** NA **Concurrent treatments:** NR	**Benefits:** YGTSS, CGI-TS, response **Harms:** Neuromotor effects, GI disorders, metabolic effects, QT	Aripiprazole is efficacious and tolerated in children and adolescents with Tourette syndrome.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	IQ ≤ 70, seizure disorders, history of neuroleptic malignant syndrome, serious brain injury, stroke, or other neurologic disorders. Secondary tic symptoms accompanied by tardive tics, Huntington disease, neuroacanthocytosis, autism. Significant medical problems. History of allergy or hypersensitivity reactions to aripiprazole, nonresponsive to antipsychotic treatment, participating in another clinical study within 1 month before screening, pregnant or lactating, female adolescents who did not consent to contraception during study and up to 8 weeks after. Requiring cognitive behavioral therapy during study period.				
Yoo et al., 2011 [91] **Country:** South Korea **Condition category:** Tic disorders	**Recruitment Dates:** August 2005 – March 2007 **Study design:** NRCT (parallel) **Diagnostic criteria:** DSM-IV, Total tic	**Enrolled:** 48 **Analyzed:** 48 **Completed:** 37 **GROUP 1:** **N:** 31 **Age, mean±SD (range):** 11.2±3.5 (6-18) yr **Males %:** 71%	**Treatment duration:** 8 wk **Run-in phase:** Yes **Run-in phase duration:** Drug free for 2 wk before study entry **Permitted drugs:** NR **Prohibited drugs:** NR	**Benefits:** YGTSS, CGI-I, CGI-S **Harms:** ESRS, AE checklist	Aripiprazole may be effective and tolerable in the treatment of children and adolescents with tic disorders. Additional controlled studies are needed to determine efficacy

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Funding: NR **Risk of Bias:** High (subjective), High (objective)	scores ≥22 on Korean version of YGTSS **Setting:** outpatient **Inclusion criteria:** Tic disorders, drug free ≥ 2 weeks before study entry, no significant medical problems **Exclusion criteria:** Current mood disorders, psychotic symptoms, AD (OCD allowed), IQ ≤ 70, previous or current seizure episodes, EEG abnormalities, previously used aripiprazole	**Caucasian %:** NR **Diagnostic breakdown (n):** Tourette syndrome (19), Chronic motor and vocal tic disorder (7), Transient tic disorder (5) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** ADHD (9), ODD (2), OCD (3) **GROUP 2:** **N:** 17 **Age, mean±SD (range):** 8.6±2.9 (6-16) yr **Males %:** 64.7% **Caucasian %:** NR **Diagnostic breakdown (n):** Tourette syndrome (7), Chronic motor and vocal tic disorder (4), Transient tic disorder (6) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** ADHD (6)	**GROUP 1** **Drug name:** Aripiprazole **Dosing variability:** Variable **Target dose (mg/day):** 20 mg/day **Daily dose (mg/day), mean±SD (range):** 10.6±5.2 (2.5-20) mg/day **Concurrent treatments:** NR **GROUP 2:** **Drug name:** Haloperidol **Dosing variability:** Variable **Target dose (mg/day):** 4.5 mg/day **Daily dose (mg/day), mean±SD (range):** 1.9±1.1 (0.75-4.5) mg/day **Concurrent treatments:** NR		and tolerability of aripiprazole in patients with tic disorders.

ABC = Aberrant Behavior Checklist; ABC-C = Aberrant Behavior Checklist-Community; ADI-R = Autism Diagnostic Interview-Revised; ADOS = Autism Diagnostic Observation Schedule; AE = Adverse Event; ASD = autism spectrum disorder; β-HCG = beta human chorionic gonadotropin; BMI = body mass index; BPRS = Brief Psychiatric Rating Scale; BPRS-A = Brief Psychiatric Rating Scale-Anchored; C-DISC 4 = Computerized Diagnostic Interview Schedule for Children, version four; CARS = Childhood Autism Rating Scale; CAS-P = Children's Aggression Scale-Parent; CAS-T = Children's Aggression Scale-Teacher; CBCL = Child Behavior Checklist; CD = conduct disorder; CDRS-R = Children's Depression Rating Scale, Revised; CGI-C = Clinical Global Impression-Change; CGI-I = Clinical Global Impressions-Improvement; CGI-S = Clinical Global Impressions-Severity; CNS = central nervous system; COPS = Criteria of Prodromal Syndromes; CPRS = Children's Psychiatric Rating Scale; day = day(s); CPT = Continuous performance task ; DBD = disruptive behavior disorder; DICA-R = Diagnostic Interview for Children and Adolescents-Revised; DSM = Diagnostic and Statistical Manual of Mental Disorders; ECG = electrocardiogram; FGA = first-generation antipsychotics; GAD = generalized anxiety disorder; HALFS = Health And Life Functioning Scale ; HIV = human immunodeficiency virus; hr = hour(s); IED = intermittent explosive disorder; IM = intramuscular; IQ = intelligence quotient; KID-SCID = childhood disorders form of the Structured Clinical Interview for DSM-IV Disorders; K-SADS = Kiddie-Schedule for Affective Disorders and Schizophrenia; K-SADS-E = Kiddie-Schedule for Affective Disorders and Schizophrenia (Epidemiological Version); K-SADS-P = Kiddie-Schedule for Affective Disorders and Schizophrenia (Present Episode Version); K-SADS-PL = Kiddie-Schedule for Affective Disorders and Schizophrenia (Present and

Lifetime Version); KQ = key question; LT = long term; MAO-I = monoamine oxidase inhibitor; MDD = major depressive disorder; mo = month(s); MVLT = Modified Version of the California Verbal Learning Test; N = number; NCBRF = Nisonger Child Behavior Rating Form; NMS = neuroleptic malignant syndrome; NOS = not otherwise specified; NR = not reported; NRCT = non-randomized controlled trial; NSAID = non-steroidal anti-inflammatory drug; OAS = Overt Aggression Scale; ODD = oppositional defiant disorder; P-LES-Q = Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire; PANSS = Positive and Negative Syndrome Scale; PDD = pervasive developmental disorder; PTSD = post-traumatic stress disorder; Q-LES-Q = Quality of Life Enjoyment and Satisfaction Questionnaire; RCT = randomized controlled trial; SA = substance abuse; SCID-I/P = Clinical Interview for DSM-IV-TR Axis I Disorders-Patient Edition; SGA = second-generation antipsychotic; SSRI = selective serotonin reuptake inhibitor; ST = short term; TBI = traumatic brain injury; TSGS = Tourette Syndrome Global Scale; TSSS = Tourette Symptom Severity Scale; VABS = Vineland Adaptive Behavior Scale; WASH-U-KSADS = Washington University in St. Louis Kiddie Schedule for Affective Disorders and Schizophrenia; WISC = Wechsler Intelligence Scale for Children; YBOCS = Yale-Brown Obsessive Compulsive Scale; YGTSS = Yale Global Tic Severity Scale; YMRS = Young Mania Rating Scale; yr = year(s)

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Appendix E. Associated Publications

Main Publication	Associated Publications
Aman MG, Marks RE, Turbott SH, et al. Clinical effects of methylphenidate and thioridazine in intellectually subaverage children. Journal of the American Academy of Child & Adolescent Psychiatry. 1991 Mar;30(2):246-56. PMID: 2016229.	Aman MG, Marks RE, Turbott SH et al. Methylphenidate and thioridazine in the treatment of intellectually subaverage children: effects on cognitive-motor performance. Journal of the American Academy of Child & Adolescent Psychiatry, 1991;30(5), 816-824.
Aman MG, De Smedt G, Derivan, A, et al. Double-blind, placebo-controlled study of risperidone for the treatment of disruptive behaviors in children with subaverage intelligence. Am J Psychiatry 2002;159(8):1337-46.	Aman M, Findling A, Derivan U. Risperidone versus placebo for severe conduct disorder in children with mental retardation. Int J Neuropsychopharmacol 2000:S144.
	Aman MG, Findling RL, Derivan AT, et al. Effects of risperidone on the behavior of children with subaverage IQ's and conduct disorder or oppositional defiant disorder. Annual Meeting of the American Psychiatric Association; 2001.
	Aman MG, Findling RL. Effects of risperidone on the behavior of children with subaverage IQ's and conduct disorder or oppositional defiant disorder. 155th Annual Meeting of the American Psychiatric Association; 2002.
	Biederman J, Mick E, Faraone SV, et al. Risperidone for the treatment of affective symptoms in children with disruptive behavior disorder: a post hoc analysis of data from a 6-week, multicenter, randomized, double-blind, parallel-arm study. Clin Ther 2006;28(5):794-800.
	Findling RL, Aman MG, Eerdekens M, et al. Long-term, open-label study of risperidone in children with severe disruptive behaviors and below-average IQ. Am J Psychiatry 2004;161(4):677-84.
	Turgay A. Risperidone in children with disruptive behavior disorder and ADHD. 154th Annual Meeting of the American Psychiatric Association; 2001.
Aman MG, Bukstein OG, Gadow KD, et al. What does risperidone add to parent training and stimulant for severe aggression in child attention-deficit/hyperactivity disorder? Journal of the American Academy of Child & Adolescent Psychiatry. 2014 Jan;53(1):47-60.e1. PMID: 24342385.	Arnold LE, Gadow KD, Farmer CA, et al. Comorbid anxiety and social avoidance in treatment of severe childhood aggression: response to adding risperidone to stimulant and parent training; mediation of disruptive symptom response. Journal of Child & Adolescent Psychopharmacology, 2015;25(3), 203-212.
	Gadow KD, Arnold, LE, Molina, BS, et al. Risperidone added to parent training and stimulant medication: effects on attention-deficit/hyperactivity disorder, oppositional defiant disorder, conduct disorder, and peer aggression. Journal of the American Academy of Child & Adolescent Psychiatry. 2014;53(9), 948-959.e941.
Arango C, Robles O, Parellada M, et al. Olanzapine compared to quetiapine in adolescents with a first psychotic episode. Eur Child Adolesc Psychiatry 2009;18(7):418-28.	Robles O, Zabala A, Bombin I, et al. Cognitive Efficacy of Quetiapine and Olanzapine in Early-Onset First-Episode Psychosis. Schizophr Bull 2009:1-11.
Arango C, Giraldez M, Merchan-Naranjo J, et al. Second-generation antipsychotic use in children and adolescents: A six-month prospective cohort study in drug-naive patients. Journal of the American Academy of Child & Adolescent Psychiatry. 2014 Nov;53(11):1179-90,90.e1-4. PMID: 25440308.	Merchan-Naranjo J, Tapia C, Bailon C, et al. Secondary effects of antipsychotic treatment in naive or quasi-naive children and adolescents: design of a follow-up protocol and baseline results. Revista de Psiquiatria y Salud Mental. 2012;5(4), 217-228.
Buitelaar JK, van der Gaag RJ, Cohen-Kettenis P, et al. A randomized controlled trial of risperidone in the treatment of aggression in hospitalized adolescents with subaverage	Buitelaar JK, van der Gaag RJ, Melman CT. Risperidone in the treatment of aggressive behaviour disorders in adolescents with mild mental retardation: a prospective, randomised, double-blind, placebo-controlled trial. Paris: 11th European College of

Main Publication	Associated Publications
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van Bruggen J, Tijssen J, Dingemans P, et al. Symptom response and side-effects of olanzapine and risperidone in young adults with recent onset schizophrenia. Int Clin Psychopharmacol 2003;18(6):341–6.	Lavalaye J, Linszen DH, Booij J, et al. Dopamine D2 receptor occupancy by olanzapine or risperidone in young patients with schizophrenia. Psychiatry Res 1999;92(1):33–44.
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Appendix F. Excluded Studies

1. Adler BA, Wink LK, Early M, et al. Drug-refractory aggression, self-injurious behavior, and severe tantrums in autism spectrum disorders: a chart review study. Autism. 2015;19(1):102-6. DOI: 10.1177/1362361314524641. PMID: 24571823.
EXCLUDE: Study Design.

2. Akkaya C, Sarandol A, Cangur S, et al. Retrospective database analysis on the effectiveness of typical and atypical antipsychotic drugs in an outpatient clinic setting. Hum Psychopharmacol. 2007;22(8):515-28. DOI: 10.1002/hup.882. PMID: 17868197.
EXCLUDE: Age.

3. Alessi NE. Ziprasidone in autism. J Am Acad Child Adol Psychiatry. 2003;42(6):622-3. DOI: http://dx.doi.org/10.1097/01.CHI.0000046853.56865.10. PMID: 12921465.
EXCLUDE: Publication Type.

4. Alfaro CL, Wudarsky M, Nicolson R, et al. Correlation of antipsychotic and prolactin concentrations in children and adolescents acutely treated with haloperidol, clozapine, or olanzapine. J Child Adol Psychopharmacol. 2002;12(2):83-91. DOI:10.1089/104454602760219126. PMID: 12188977.
EXCLUDE: Study Design.

5. Aman M, Buitelaar J, Smedt GD, et al. Pharmacotherapy of disruptive behavior and item changes on a standardized rating scale: pooled analysis of risperidone effects in children with subaverage IQ. J Child Adol Psychopharmacol. 2005;15(2):220-32. DOI:10.1089/cap.2005.15.220. PMID: 15910206.
EXCLUDE: Outcomes.

6. Aman M, Rettiganti M, Nagaraja HN, et al. Tolerability, safety, and benefits of risperidone in children and adolescents with autism: 21-month follow-up after 8-week placebo-controlled trial. J Child Adol Psychopharmacol. 2015;25(6):482-93. doi: http://dx.doi.org/10.1089/cap.2015.0005. PMID: 26262903.
EXCLUDE: Intervention.

7. Aman MG, Kasper W, Manos G, et al. Line-item analysis of the Aberrant Behavior Checklist: results from two studies of aripiprazole in the treatment of irritability associated with autistic disorder. J Child Adol Psychopharmacol. 2010;20(5):415-22. doi: http://dx.doi.org/10.1089/cap.2009.0120. PMID: 20973712. EXCLUDE: Outcomes.

8. Aman MG, White AJ. Thioridazine dose effects with reference to stereotypic behavior in mentally retarded residents. J Autism Dev Disord. 1988;18(3):355-66. doi: http://dx.doi.org/10.1007/BF02212192. PMID: 1988228303.
EXCLUDE: Intervention.

9. Amann BL, Pogarell O, Mergl R, et al. EEG abnormalities associated with antipsychotics: a comparison of quetiapine, olanzapine, haloperidol and healthy subjects. Hum Psychopharmacol. 2003;18(8):641-6. DOI: 10.1002/hup.537. PMID: 14696024.
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10. Andrade SE, Lo JC, Roblin D, et al. Antipsychotic medication use among children and risk of diabetes mellitus. Pediatrics. 2011;128(6):1135-41. DOI: http://dx.doi.org/10.1542/peds.2011-0855. PMID: 22106077.
EXCLUDE: Intervention.

11. Andrezina R, Josiassen RC, Marcus RN, et al. Intramuscular aripiprazole for the treatment of acute agitation in patients with schizophrenia or schizoaffective disorder: a double-blind, placebo-controlled comparison with intramuscular haloperidol. Psychopharmacology. 2006;188(3):281-92. DOI: 10.1007/s00213-006-0541-xPMID: 16953381.
EXCLUDE: Age.

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13. Arato M, O'Connor R, Meltzer HY, et al. A 1-year, double-blind, placebo-controlled trial of ziprasidone 40, 80 and 160 mg/day in chronic schizophrenia: the Ziprasidone Extended Use in Schizophrenia (ZEUS) study. Int Clin Psychopharmacol. 2002;17(5):207-15. PMID: 12177583.

EXCLUDE: Age.

14. Aripiprazole and adolescent schizophrenia: a simple neuroleptic. No comparison with standard neuroleptic in adolescents. Prescrire Int. 2009;18(104):251. PMID: 20025091.
EXCLUDE: Publication Type.

15. Aripiprazole and adolescent schizophrenia: a simple neuroleptic. No comparison with standard neuroleptic in adolescents. Prescrire Int. 2009;18(104):251. PMID: 20025091.
EXCLUDE: Publication Type.

16. Aripiprazole at adult doses effective in youths with schizophrenia. Brown University Child & Adolescent Psychopharmacology Update. 2008;10(11):1-7. PMID: N/A.
EXCLUDE: Outcomes.

17. Aripiprazole effective in treating irritability in autistic youth. Brown University Child & Adolescent Psychopharmacology Update. 2010;12(2):4-5. PMID: N/A.
EXCLUDE: Publication Type.

18. Armour A, Gottschlich MM, Khoury J, et al. A randomized, controlled prospective trial of zolpidem and haloperidol for use as sleeping agents in pediatric burn patients. J Burn Care Res. 2008;29(1):238-47. doi: http://dx.doi.org/10.1097/BCR.0b013e31815f384e. PMID: 18182928.
EXCLUDE: Diagnosis.

19. Arranz B, San L, Duenas RM, et al. Lower weight gain with the orally disintegrating olanzapine than with standard tablets in first-episode never treated psychotic patients. Hum Psychopharmacol. 2007;22(1):11-5. DOI: 10.1002/hup.819. PMID: 17191265.
EXCLUDE: Age.

20. Arvanitis LA, Miller BG. Multiple fixed doses of "Seroquel" (quetiapine) in patients with acute exacerbation of schizophrenia: a comparison with haloperidol and placebo. The Seroquel Trial 13 Study Group. Biol Psychiatry. 1997;42(4):233-46. DOI: http://dx.doi.org/10.1016/S0006-3223(97)00190-X PMID: 9270900.
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21. Atmaca M, Kuloglu M, Tezcan E, et al. Quetiapine is not associated with increase in prolactin secretion in contrast to haloperidol. Arch Med Res. 2002;33(6):562-5. DOI: http://dx.doi.org/10.1016/S0188-4409(02)00403-4 PMID: 12505103.
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EXCLUDE: Age.

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EXCLUDE: Study Design.

Appendix G. Additional Results from Network Meta-analysis and General Adverse Effects

Figure G1. Network Meta-Analysis Star Plot: Weight
Figure G2. Inconsistency Factor Plot: Weight
Figure G3. Network Meta-Analysis Star Plot: BMI
Figure G4. Inconsistency Factor Plot: BMI

Table G1: Results for all possible comparisons from network meta-analysis: weight
Table G2: Results for all possible comparisons from network meta-analysis: BMI

Table G3: Findings for GAE: FGA vs SGA
Table G4: Findings for GAE: FGA vs FGA
Table G5: Findings for GAE: SGA vs SGA
Table G6: Findings for GAE: Dose Comparisons - Aripiprazole
Table G7. Findings for GAE: Dose Comparisons - Asenapine
Table G8. Findings for GAE: Dose Comparisons - Paliperidone
Table G9. Findings for GAE: Dose Comparisons - Quetiapine
Table G10. Findings for GAE: Dose Comparisons - Risperidone
Table G11. Findings for GAE: Dose Comparisons - Ziprasidone
Table G12. Findings for GAE: FGA vs Placebo
Table G13. Findings for GAE: SGA vs Placebo

Figure G1. Network Meta-Analysis Star Plot: Weight

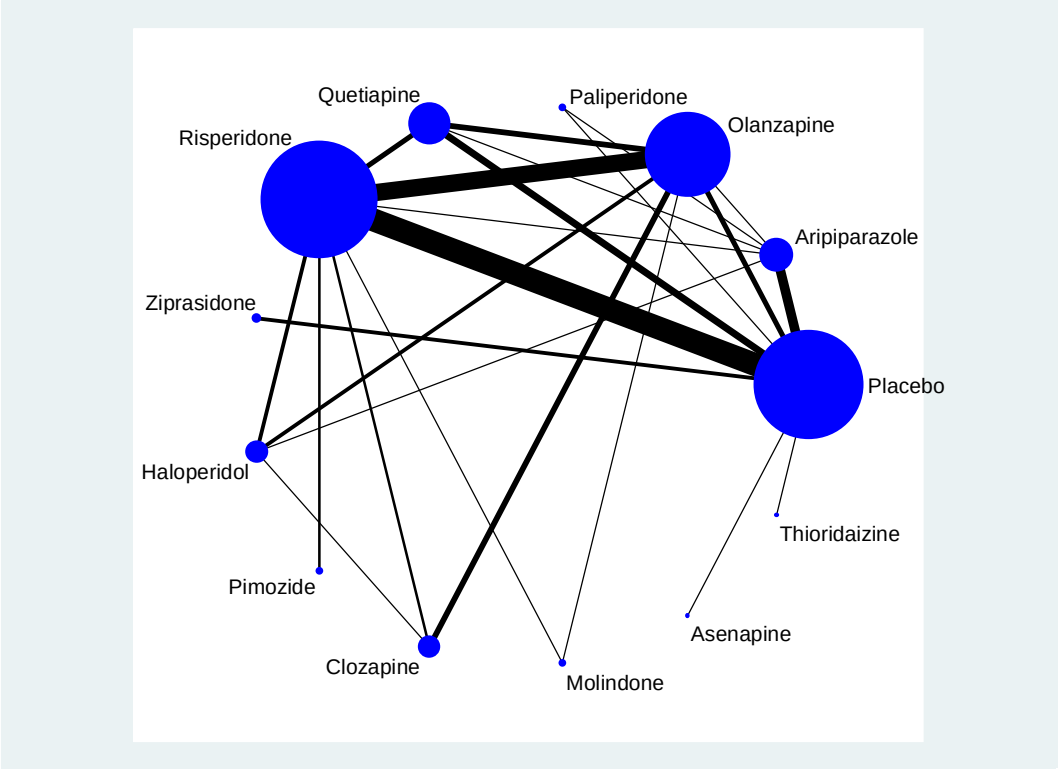
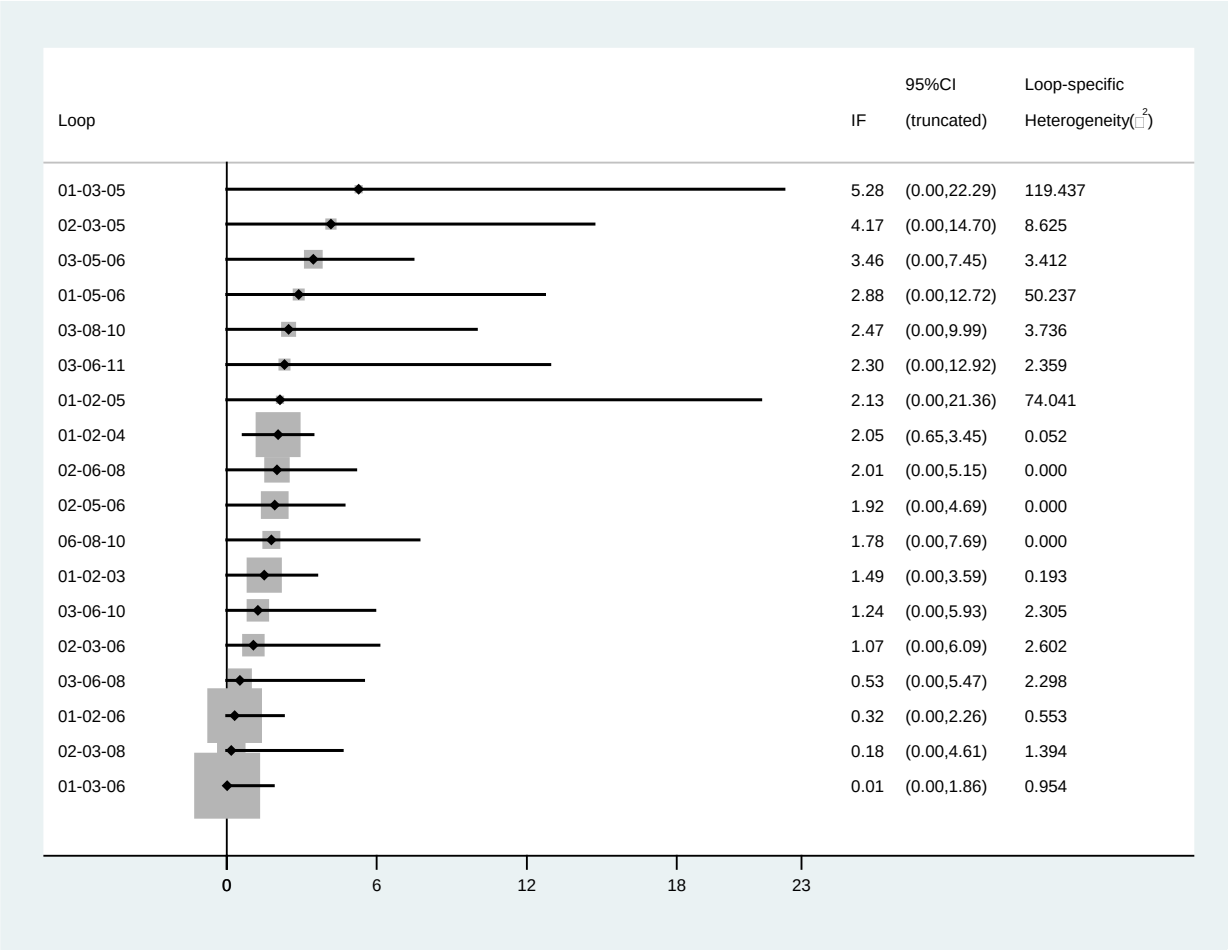


Figure G2. Inconsistency Factor Plot: Weight



1 Placebo
2 Aripiprazole
3 Olanzapine
4 Paliperidone
5 Quetiapine
6 Risperidone
7 Ziprasidone
8 Haloperidol
9 Pimozide
10 Clozapine
11 Molindone
12 Asenapine
13 Thioridazine

Figure G3. Network Meta-Analysis Star Plot: BMI

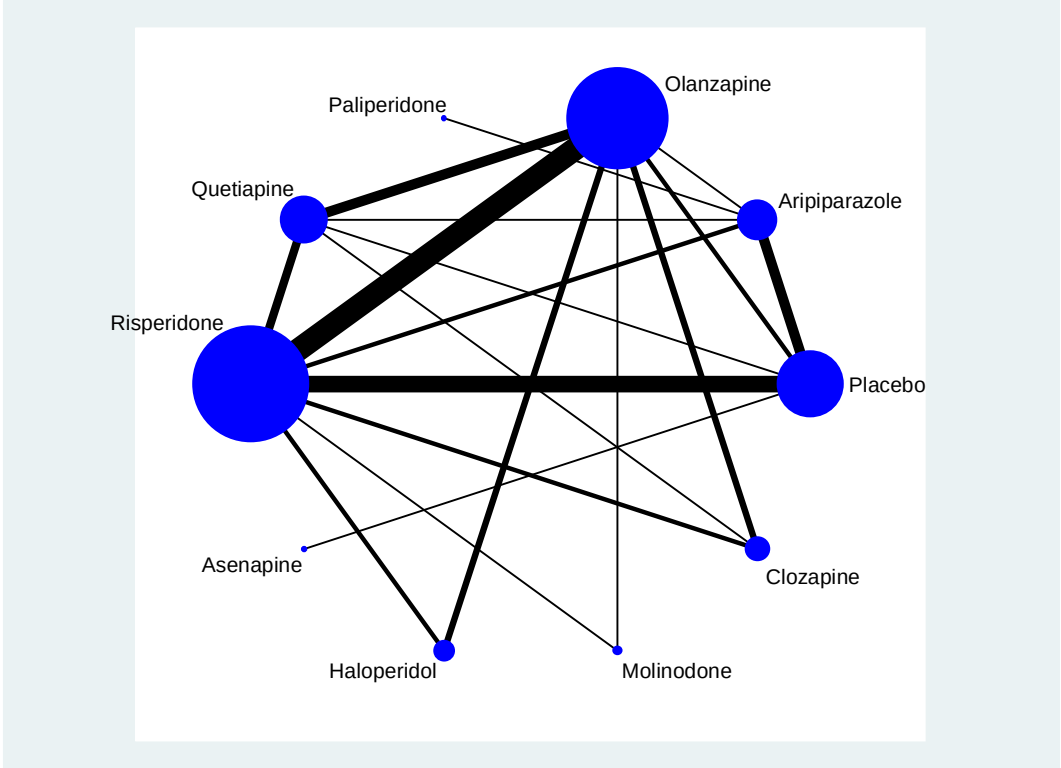
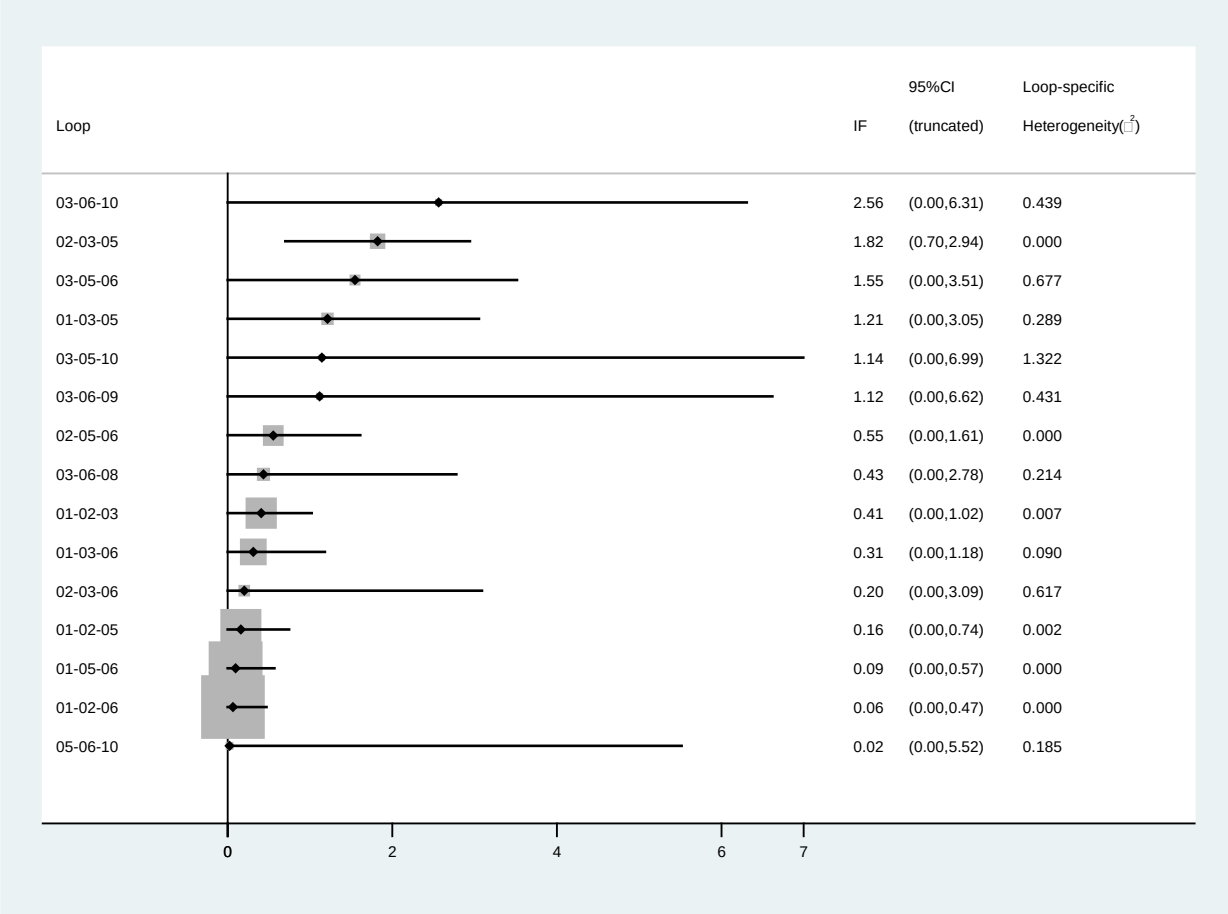


Figure G4. BMI Inconsistency Factor Plot



1. Placebo
2. Aripiprazole
3. Olanzapine
4. Paliperidone
5. Quetiapine

6. Risperidone
7. Asenapine
8. Haloperidol
9. Molindone
10. Clozapine

Table G1: Results for all possible comparisons from network meta-analysis: weight

Table G2: Results for all possible comparisons from network meta-analysis: BMI

	Placebo	Aripiprazole	Olanzapine	Paliperidone	Quetiapine	Risperidone	Ziprasidone	Haloperidol	Pimozide	Clozapine	Molindone	Asenapine
Aripiprazole	0.82 (0.25, 1.40)											
Olanzapine	4.10 (3.42, 4.85)	3.28 (2.44, 4.18)										
Paliperidone	1.69 (0.36, 3.08)	0.87 (-0.49, 2.26)	-2.41 (-3.95 -0.91)									
Quetiapine	1.26 (0.52, 1.96)	0.44 (-0.49, 1.31)	-2.84 (-3.87,-1.93)	-0.43 (-2.02, 1.06)								
Risperidone	1.84 (1.40, 2.34)	1.02 (0.33, 1.75)	-2.26 (-2.96,-1.58)	0.15 (-1.29, 1.58)	0.58 (-0.20, 1.45)							
Ziprasidone	-0.10 (-1.23, 1.03)	-0.93 (-2.20, 0.34)	-4.21 (-5.59,-2.90)	-1.80 (-3.59,-0.05)	-1.37 (-2.68,-0.00)	-1.95 (-3.19,-0.75)						
Haloperidol	0.95 (-0.45, 2.34)	0.12 (-1.27, 1.51)	-3.16 (-4.62,-1.75)	-0.75 (-2.69, 1.15)	-0.32 (-1.85, 1.25)	-0.90 (-2.34, 0.51)	1.05 (-0.76, 2.86)					
Pimozide	0.51 (-8.83, 9.89)	-0.32, (-9.71, 9.08)	-3.60 (-13.02, 5.76)	-1.19 (-10.70, 8.29)	-0.75 (-10.16, 8.67)	-1.34 (-10.72, 8.03)	0.61 (-8.82, 10.08)	-0.45 (-9.92, 9.02)				
Clozapine	2.39 (0.40, 4.38)	1.57 (-0.46, 3.60)	-1.71 (-3.67, 0.21)	0.70 (-1.69, 3.08)	1.14 (-0.95, 3.24)	0.55 (-1.43, 2.50)	2.50 (0.22, 4.79)	1.45 (-0.77, 3.67)	1.88 (-7.65, 11.58)			
Molindone	-0.70 (-7.19, 5.85)	-1.55 (-8.11, 5.05)	-4.83 (-11.34, 1.73)	-2.42 (-9.09, 4.30)	-1.98 (-8.56, 4.65)	-2.57 (-9.10, -3.99)	-0.61 (-7.26, 6.07)	-1.66 (-8.33, 5.06)	-1.25 (-12.55, 10.35)	-3.11 (-9.96, 3.70)		
Asenapine	1.12 (-0.63, 2.86)	0.30 (-1.54, 2.13)	-2.98 (-4.92,-1.15)	-0.57 (-2.80, 1.61)	-0.15 (-2.00, 1.77)	-0.72 (-2.57, 1.05)	1.22 (-0.85, 3.30)	0.17 (-2.06, 2.41)	0.61 (-8.94, 10.14)	-1.28 (-3.93, 1.34)	1.83 (-4.97, 8.60)	
Thiroidazine	0.13 (-1.69, 1.94)	-0.70 (-2.59, 1.21)	-3.97 (-5.96,-2.08)	-1.57 (-3.86, 0.67)	-1.13 (-3.06, 0.84)	-1.71 (-3.61, 0.13)	0.23 (-1.90, 2.36)	-0.82 (-3.11, 1.47)	-0.37 (-9.94, 9.18)	-2.27 (-4.95, 0.40)	0.85 (-5.98, 7.63)	-0.99 (-3.51, 1.54)

	Placebo	Aripiprazole	Olanzapine	Paliperidone	Quetiapine	Risperidone	Asenapine	Haloperidol	Molindone
Aripiprazole	0.28 (0.09, 0.51)								
Olanzapine	1.54 (1.30, 1.89)	1.26 (0.97, 1.64)							
Paliperidone	0.99 (0.39, 1.61)	0.70 (0.13, 1.28)	-0.55 (-1.27, 0.06)						
Quetiapine	0.43 (0.02,	0.15 (-0.32,	-1.11 (-1.66,	-0.56 (-1.32,					

	0.72)	0.48)	-0.74)	0.07)					
Risperidone	0.58 (0.39, 0.81)	0.30 (0.03, 0.57)	-0.96 (-1.27, -0.71)	-0.41 (-1.04, 0.23)	0.15 (-0.16, 0.60)				
Asenapine	0.53 (0.05, 1.01)	0.24 (-0.29, 0.75)	-1.01 (-1.65, -0.53)	-0.46 (-1.24, 0.30)	0.09 (-0.42, 0.76)	-0.06 (-0.60, 0.45)			
Haloperidol	-0.40 (-1.48, 0.68)	-0.69 (-1.74, 0.41)	-1.96 (-2.99, -0.89)	-1.39 (-2.58, -0.16)	-0.82 (-1.89, 0.33)	-0.99 (-2.01, 0.09)	-0.92 (-2.06, 0.26)		
Molindone	0.25 (-2.03, 2.55)	-0.03 (-2.29, 2.28)	-1.29 (-3.54, 1.00)	-0.73 (-3.05, 1.64)	-0.16 (-2.43, 2.18)	-0.32 (-2.58, 1.97)	-0.26 (-2.57, 2.09)	0.66 (-1.82, 3.14)	
Clozapine	1.98 (0.57, 3.39)	1.70 (0.28, 3.14)	0.43 (-0.99, 1.86)	0.99 (-0.54, 2.55)	1.57 (0.14, 3.03)	1.40 (-0.00, 2.82)	1.46 (-0.02, 2.97)	2.37 (0.62, 4.14)	1.73 (-0.98, 4.36)

Table G2. Findings for GAE: FGA versus SGA

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
FGA vs. SGA	Any AE	3, 204	89	97	86	107	RR, 1.16; 95% CrI, 0.71 to 1.92[1, 2]
	Any AE (6to<12)	2, 74	17 17	20 20	15 13	21 13	RR, 1.19; 95% CI, 0.56 to 1.65[1] RR, 0.86; 95% CI, 0.70 to 1.07[1]
	AE limiting treatment	5, 269 2, 101	36	127	21	142	RR, 1.82; 95% CrI, 0.90 to 4.42[1-3] Not estimable[4]
	AE limiting treatment (12+)	5, 234	13	127	27	107	RR, 0.42; 95% CrI, 0.11 to 1.19[1, 5]
	Any EPS	4, 110	16	37	13	73	RR, 2.59; 95% CrI, 1.00 to 7.00[4, 6, 7]
	Akathisia	4, 115	10	44	3	71	RR, 4.30; 95% CrI, 0.93 to 22.71[3, 4]
	Dystonia	4, 115	8	44	1	71	RR, 6.53; 95% CrI, 1.29 to 34.18[3, 4]
	Weight (kg)	13, 432	NA	154	NA	278	MD, -2.67; 95% CrI, -4.61 to -0.70[1-4, 6, 8-12]
	Weight (kg) (6to<12)	2, 54	NA NA	10 10	NA NA	13 21	MD, -3.50; 95% CI, -10.24 to 3.24[1] MD, -3.40; 95% CI, -9.92 to 3.12[1]
	BMI ($kg \cdot m^{-2}$)	7, 236	NA	73	NA	163	MD, -1.57; 95% CrI, -2.49 to -0.53[1, 3, 4, 13]
	BMI ($kg \cdot m^{-2}$) (6to<12)	2, 54	NA NA	10 10	NA NA	13 21	MD, -0.70; 95% CI, -3.08 to 1.68[1] MD, -0.80; 95% CI, -3.15 to 1.55[1]
	≥7% increase in weight, see haloperidol vs. olanzapine	2, 41					
	Increased total cholesterol, see various FGA's vs. various SGA's	1, 48					
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides, see various FGA's vs. various SGA's	1, 48					
	Increased fasting glucose, see various FGA's vs. various SGA's	1, 48					
	Sedation	6, 271	38	124	46	147	RR, 1.05; 95% CrI, 0.75 to 1.89[1, 3, 4]
	Sedation (6to<12)	2, 74	5 5	20 20	2 3	21 13	RR, 2.63; 95% CI, 0.57 to 12.02[1] RR, 1.08; 95% CI, 0.31 to 3.78[1]
	Sedation (12+)	3, 160	18	87	5	73	RR, 2.84; 95% CrI, 0.34 to 92.81[5]

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
	Somnolence	3, 83	15	41	26	42	RR, 0.53; 95% CrI, 0.14 to 1.75[6, 9, 12]
	Hyperprolactinemia	2, 45	9 9	10 10	0 7	15 10	RR, 27.64; 95% CI, 1.79 to 427.25[14] RR, 1.29; 95% CI, 0.82 to 2.03[14]
	Hyperprolactinemia (12+)	3, 160	0 0 0	29 29 29	0 2 6	28 12 33	Not estimable[5] RR, 0.09; 95% CI, 0.00 to 1.68[5] RR, 0.09; 95% CI, 0.01 to 1.48[5]
	Prolactin-related events	3, 106	14	50	13	56	RR, 1.20; 95% CrI, 0.39 to 3.85[3, 15]
	Prolactin-related events (12+)	3, 160	0 0 0	29 29 29	0 0 1	28 12 33	Not estimable[5] Not estimable[5] RR, 0.38; 95% CI, 0.02 to 8.93[5]
Haloperidol vs. aripiprazole	Any AE	1, 48	17	17	25	31	RR, 1.22; 95% CI, 1.01 to 1.48[2]
	AE limiting treatment	1, 48	6	17	5	31	RR, 2.19; 95% CI, 0.78 to 6.12[2]
	Any EPS	1, 48	7	17	6	31	RR, 2.13; 95% CI, 0.85 to 5.32[2]
	Akathisia	0					
	Dystonia	0					
	Weight (kg)	1, 48	NA	17	NA	31	MD, 0.40; 95% CI, -0.41 to 1.21[2]
	BMI ($kg \cdot m^{-2}$)	0					
	≥7% increase in weight	0					
	Increased total cholesterol	0					
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	0					
	Increased fasting glucose	0					
	Sedation	0					
	Somnolence	0					
	Hyperprolactinemia	0					
	Prolactin-related events	0					
Haloperidol vs. clozapine	Any AE	0					
	AE limiting treatment	0					
	AE limiting treatment (12+)	1, 57	1	29	4	28	RR, 0.24; 95% CI, 0.03 to 2.03[5]
	Any EPS	0					
	Akathisia	0					

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
	Dystonia	0					
	Weight (kg)	1, 21	NA	11	NA	10	MD, 0.04; 95% CI, -4.32 to 4.40[12]
	BMI ($kg \cdot m^{-2}$)	0					
	≥7% increase in weight	0					
	Increased total cholesterol	0					
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	0					
	Increased fasting glucose	0					
	Sedation	0					
	Sedation (12+)	1, 57	6	29	4	28	RR, 1.45; 95% CI, 0.46 to 4.59[5]
	Somnolence	1, 21	3	11	9	10	RR, 0.30; 95% CI, 0.11 to 0.81[12]
	Hyperprolactinemia	1, 25	9	10	0	15	RR, 27.64; 95% CI, 1.79 to 427.25[14]
	Hyperprolactinemia (12+)	1, 57	0	29	0	28	Not estimable[5]
	Prolactin-related events	0					
	Prolactin-related events (12+)	1, 57	0	29	0	28	Not estimable[5]
Haloperidol vs. olanzapine	Any AE	0					
	AE limiting treatment	2, 57	0 7	7 15	0 0	19 16	Not estimable[4] RR, 15.94; 95% CI, 0.99 to 256.93[3]
	AE limiting treatment (12+)	1, 41	1	29	4	12	RR, 0.10; 95% CI, 0.01 to 0.83[5]
	Any EPS	2, 38	1 4	6 7	0 3	6 19	RR, 3.00; 95% CI, 0.15 to 61.74[6] RR, 3.62; 95% CI, 1.07 to 12.27[4]
	Akathisia	2, 57	3 2	7 15	0 2	19 16	RR, 17.50; 95% CI, 1.01 to 301.78[4] RR, 1.07; 95% CI, 0.17 to 6.64[3]
	Dystonia	2, 57	2 2	7 15	0 0	19 16	RR, 12.50; 95% CI, 0.67 to 232.59[4] RR, 5.31; 95% CI, 0.28 to 102.38[3]
	Weight (kg)	3, 61	NA	18	NA	43	MD, -3.87; 95% CrI, -11.3 to 2.80[3, 4, 6]
	BMI ($kg \cdot m^{-2}$)	3, 69	NA	22	NA	47	MD, -1.87; 95% CrI, -4.36 to 0.93[3, 4, 13]
	≥7% increase in weight	2, 41	2 1	6 8	6 19	6 21	RR, 0.38; 95% CI, 0.14 to 1.06[6] RR, 0.14; 95% CI, 0.02 to 0.87[4]
	Increased total	0					

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
	cholesterol						
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	0					
	Increased fasting glucose	0					
	Sedation	2, 57	3 14	7 15	9 15	19 16	RR, 0.90; 95% CI, 0.34 to 2.41[4] RR, 1.00; 95% CI, 0.83 to 1.20[3]
	Sedation (12+)	1, 41	6	29	0	12	RR, 5.63; 95% CI 0.34 to 92.81[5]
	Somnolence	1, 12	2	6	5	6	RR, 0.40; 95% CI, 0.12 to 1.31[6]
	Hyperprolactinemia	1, 20	9	10	7	10	RR, 1.29; 95% CI, 0.82 to 2.03[14]
	Hyperprolactinemia (12+)	1, 41	0	29	2	12	RR, 0.09; 95% CI, 0.00 to 1.68[5]
	Prolactin-related events	1, 31	4	15	3	16	RR, 1.42; 95% CI, 0.38 to 5.33[3]
	Prolactin-related events (12+)	1, 41	0	29	0	12	Not estimable[5]
Haloperidol vs. risperidone	Any AE	0					
	AE limiting treatment	2, 58	0 7	7 15	0 5	17 19	Not estimable[4] RR, 1.77; 95% CI, 0.70 to 4.48[3]
	AE limiting treatment (12+)	1, 62	1	29	9	33	RR, 0.13; 95% CI, 0.02 to 0.94[5]
	Any EPS	1, 24	4	7	4	17	RR, 2.43; 95% CI, 0.83 to 7.08[4]
	Akathisia	2, 58	3 2	7 15	1 0	17 19	RR, 7.29; 95% CI, 0.91 to 58.61[4] RR, 6.25; 95% CI, 0.32 to 121.14[3]
	Dystonia	2, 58	2 2	7 15	1 0	17 19	RR, 4.86; 95% CI, 0.52 to 45.32[4] RR, 6.25; 95% CI, 0.32 to 121.14[3]
	Weight (kg)	3, 81	NA	26	NA	55	MD, -2.02; 95% CrI, -9.40 to 6.30[3, 4, 8]
	BMI ($kg \cdot m^{-2}$)	2, 51	NA NA	4 7	NA NA	21 19	MD, -1.00; 95% CI, -2.47 to 0.47[4] MD, -0.40; 95% CI, -8.03 to 7.23[3]
	≥7% increase in weight	0					
	Increased total cholesterol	0					
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	0					

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
	Increased fasting glucose	0					
	Sedation	2, 58	3 14	7 15	3 17	17 19	RR, 2.43; 95% CI, 0.64 to 9.24[4] RR, 1.04; 95% CI, 0.85 to 1.28[3]
	Sedation (12+)	1, 62	6	29	1	33	RR, 6.83; 95% CI, 0.87 to 53.43[5]
	Somnolence	0					
	Hyperprolactinemia	0					
	Hyperprolactinemia (12+)	1, 62	0	29	6	33	RR, 0.09; 95% CI, 0.01 to 1.48[5]
	Prolactin-related events	2, 75	4 6	15 20	4 6	19 21	RR, 1.27; 95% CI, 0.38 to 4.24[3] RR, 1.05; 95% CI, 0.41 to 2.72[15]
	Prolactin-related events (12+)	1, 62	0	29	1	33	RR, 0.38; 95% CI, 0.02 to 8.93[5]
Molindone vs. olanzapine	Any AE	1, 75	36	40	26	35	RR, 1.21; 95% CI, 0.97 to 1.51[1]
	Any AE (6to<12)	1, 33	17	20	13	13	RR, 0.86; 95% CI, 0.70 to 1.07[1]
	AE limiting treatment	1, 75	8	40	6	35	RR, 1.17; 95% CI 0.45 to 3.04[1]
	AE limiting treatment (12+)	1, 33	5	20	3	13	RR, 1.08; 95% CI, 0.31 to 3.78[1]
	Any EPS	0					
	Akathisia	0					
	Dystonia	0					
	Weight (kg)	1, 55	NA	20	NA	35	MD, -5.80; 95% CI, -7.54 to -4.06[1]
	Weight (kg) (6to<12)	1, 23	NA	10	NA	13	MD, -3.50; 95% CI, -10.24 to 3.24[1]
	BMI ($kg \cdot m^{-2}$)	1, 55	NA	20	NA	35	MD, -2.05; 95% CI, -2.73 to -1.37[1]
	BMI ($kg \cdot m^{-2}$) (6to< 12)	1, 23	NA	10	NA	13	MD, -0.70; 95% CI, -3.08 to 1.68[1]
	≥7% increase in weight	0					
	Increased total cholesterol	0					
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	0					
	Increased fasting glucose	0					
	Sedation	1, 75	2	40	1	35	RR, 1.75; 95% CI, 0.17 to 18.48[1]
	Sedation (6to<12)	1, 33	5	20	3	13	RR, 1.08; 95% CI, 0.31 to 3.78[1]
	Somnolence	0					

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
	Hyperprolactinemia	0					
	Prolactin-related events	0					
Molindone vs. risperidone	Any AE	1, 81	36	40	35	41	RR, 1.05; 95% CI, 0.90 to 1.24[1]
	Any AE (6to<12)	1, 41	17	20	15	21	RR, 1.19; 95% CI, 0.86 to 1.65[1]
	AE limiting treatment	1, 81	8	40	5	41	RR, 1.64; 95% CI, 0.59 to 4.59[1]
	AE limiting treatment (12+)	1, 41	5	20	7	21	RR, 0.75; 95% CI, 0.28 to 1.98[1]
	Any EPS	0					
	Akathisia	0					
	Dystonia	0					
	Weight (kg)	1, 61	NA	20	NA	41	MD, -3.30; 95% CI, -5.06 to -1.54[1]
	Weight (kg) (6to<12)	1, 31	NA	10	NA	21	MD, -3.40; 95% CI, -9.92 to 3.12[1]
	BMI ($kg \cdot m^{-2}$)	1, 61	NA	20	NA	41	MD, -1.15; 95% CI, -1.87 to -0.43[1]
	BMI ($kg \cdot m^{-2}$) (6to<12)	1, 31	NA	10	NA	21	MD, -0.80; 95% CI, -3.15 to 1.55[1]
	≥7% increase in weight	0					
	Increased total cholesterol	0					
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	0					
	Increased fasting glucose	0					
	Sedation	1, 81	2	40	1	41	RR, 2.05; 95% CI, 0.19 to 21.72[1]
	Sedation (6to<12)	1, 41	5	20	2	21	RR, 2.63; 95% CI, 0.57 to 12.02[1]
	Somnolence	0					
	Hyperprolactinemia	0					
	Prolactin-related events	0					
Pimozide vs. risperidone	Any AE	0					
	AE limiting treatment	0					
	Any EPS	0					
	Akathisia	0					
	Dystonia	0					
	Weight (kg)	2, 57	NA NA	7 19	NA NA	12 19	MD, -1.80; 95% CI, -18.53 to 14.93[9] MD, -0.90; 95% CI, -12.31 to 10.51[10]
	BMI ($kg \cdot m^{-2}$)	0					

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
	≥7% increase in weight	0					
	Increased total cholesterol	0					
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	0					
	Increased fasting glucose	0					
	Sedation	0					
	Somnolence	1, 50	10	24	12	26	RR, 0.90; 95% CI, 0.48 to 1.69[9]
	Hyperprolactinemia	0					
	Prolactin-related events	0					
Various FGA's vs various SGA's	Any AE	0					
	AE limiting treatment	0					
	Any EPS	0					
	Akathisia	0					
	Dystonia	0					
	Weight (kg)	1, 48	NA	16	NA	32	MD, -2.80; 95% CI, -5.33 to -0.27[11]
	BMI ($kg \cdot m^{-2}$)	0					
	≥7% increase in weight	0					
	Increased total cholesterol	1, 48	1	16	3	32	RR, 0.67; 95% CI, 0.08 to 5.91[11]
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	1, 48	3	16	1	32	RR, 6.00; 95% CI, 0.68 to 53.19[11]
	Increased fasting glucose	1, 48	0	16	0	32	Not estimable[11]
	Sedation	0					
	Somnolence	0					
	Hyperprolactinemia	0					
	Prolactin-related events	0					

AE = adverse event; BMI = body mass index; CI = confidence interval; EPS = extrapyramidal symptoms;FGA = first generation antipsychotic; G1 = group 1; G2 = group 2; HDL = high density lipoprotein; LDL = low density lipoprotein; MD = mean difference; N = number; NA = not applicable; RR = risk ratio; SGA = second generation antipsychotic

Table G3. Findings for GAE: FGA versus FGA

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
FGA vs. FGA	Any AE	0					
	AE limiting treatment, see haloperidol vs. pimozide	1, 44					
	Any EPS	0					
	Akathisia	0					
	Dystonia	0					
	Weight (kg)	0					
	BMI ($kg \cdot m^{-2}$)	0					
	≥7% increase in weight	0					
	Increased total cholesterol	0					
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	0					
	Increased fasting glucose	0					
	Sedation (6to<12), see haloperidol continuous vs. haloperidol discontinuous	1, 120					
	Somnolence	0					
	Hyperprolactinemia	0					
	Prolactin-related events	0					
Haloperidol continuous vs. haloperidol discontinuous	Any AE	0					
	AE limiting treatment	0					
	Any EPS	0					
	Akathisia	0					
	Dystonia	0					
	Weight (kg)	0					
	BMI ($kg \cdot m^{-2}$)	0					
	≥7% increase in weight	0					
	Increased total	0					

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
	cholesterol						
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	0					
	Increased fasting glucose	0					
	Sedation (6to<12)	1, 120	0	60	0	60	Not estimable[16]
	Somnolence	0					
	Hyperprolactinemia	0					
	Prolactin-related events	0					
Haloperidol vs. pimozide	Any AE	0					
	AE limiting treatment	1, 44	9	22	3	22	RR, 3.00; 95% CI, 0.94 to 9.62[17]
	Any EPS	0					
	Akathisia	0					
	Dystonia	0					
	Weight (kg)	0					
	BMI ($kg \cdot m^{-2}$)	0					
	≥7% increase in weight	0					
	Increased total cholesterol	0					
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	0					
	Increased fasting glucose	0					
	Sedation	0					
	Somnolence	0					
	Hyperprolactinemia	0					
	Prolactin-related events	0					

AE = adverse event; BMI = body mass index; CI = confidence interval; EPS = extrapyramidal symptoms;FGA = first generation antipsychotic; G1 = group 1; G2 = group 2; HDL = high density lipoprotein; LDL = low density lipoprotein; MD = mean difference; N = number; NA = not applicable; RR = risk ratio

Table G4. Findings for GAE: SGA versus SGA

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
Aripiprazole vs. Olanzapine	Any AE	0					
	AE limiting treatment	1, 124	4	66	1	58	RR, 3.52; 95% CI, 0.40 to 30.56[18]
	Any EPS	0					
	Akathisia	1, 124	5	66	3	58	RR, 1.46; 95% CI, 0.37 to 5.86[18]
	Dystonia	0					
	Weight (kg)	1, 99	NA	47	NA	52	MD, -4.12; 95% CI, -5.50 to -2.74[18]
	BMI ($kg \cdot m^{-2}$)	1, 99	NA	47	NA	52	MD, -1.34; 95% CI, -1.85 to -0.83[18]
	≥7% increase in weight	1, 86	24	41	38	45	RR, 0.69; 95% CI, 0.52 to 0.92[18]
	Increased total cholesterol	0					
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	0					
	Increased fasting glucose	0					
	Sedation	0					
	Somnolence	0					
	Hyperprolactinemia	0					
	Prolactin-related events	0					
Aripiprazole vs. Paliperidone	Any AE	1, 227	76	114	87	113	RR, 0.87; 95% CI, 0.73 to 1.02[19]
	AE limiting treatment	1, 228	0	115	5	113	RR, 0.09; 95% CI, 0.00 to 1.60[19]
	Any EPS	0					
	Akathisia	0					
	Akathesia (6to<12)	1, 226	6	114	7	112	RR, 0.84; 95% CI, 0.29 to 2.43[19]
	Dystonia	0					
	Weight (kg)	1, 226	NA	114	NA	112	MD, -1.28; 95% CI, -1.95 to -0.61[19]
	Weight (kg) (6to<12)	1, 226	NA	114	NA	112	MD, -1.90; 95% CI, -2.96 to -0.84[19]
	BMI ($kg \cdot m^{-2}$)	1, 226	NA	114	NA	112	MD, -0.50; 95% CI, -0.74 to -0.26[19]
	BMI ($kg \cdot m^{-2}$) (6to<12)	1, 226	NA	114	NA	112	MD, -0.70; 95% CI, -1.07 to -0.33[19]
	≥7% increase in weight	0					
	≥7% increase in weight (6to<12)	1, 226	20	114	29	112	RR, 0.68; 95% CI, 0.41 to 1.12[19]
	Increased total cholesterol	0					

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	0					
	Increased fasting glucose	0					
	Sedation	1, 227	3	114	6	113	RR, 0.50; 95% CI, 0.13 to 1.93[19]
	Somnolence	1, 227	12	114	12	113	RR, 0.99; 95% CI, 0.47 to 2.11[19]
	Hyperprolactinemia	0					
	Hyperprolactinemia (6to<12)	1, 227	5	114	59	113	RR, 0.04; 95% CI, 0.02 to 0.11[19]
	Prolactin-related events	0					
Aripiprazole vs. Quetiapine	Any AE	0					
	Any AE (6to<12)	1, 73	25	62	10	11	RR, 0.44; 95% CI, 0.31 to 0.63[20]
	AE limiting treatment	1, 132	4	66	0	66	RR, 9.00; 95% CI,0.49 to 163.90[18]
	Any EPS	0					
	Akathisia	1, 132	5	66	1	66	RR, 5.00; 95% CI, 0.60 to 41.65[18]
	Akathesia (6to<12)	1, 73	5	62	1	11	RR, 0.89; 95% CI, 0.11 to 6.88[20]
	Dystonia	0					
	Weight (kg)	1, 92	NA	47	NA	45	MD, -1.63; 95% CI, -3.01 to -0.25[18]
	BMI ($kg \cdot m^{-2}$)	1, 92	NA	47	NA	45	MD, -0.45; 95% CI, -0.96 to 0.06[18]
	≥7% increase in weight	1, 77	24	41	20	36	RR, 1.05; 95% CI, 0.71 to 1.56[18]
	Increased total cholesterol	0					
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	0					
	Increased fasting glucose	0					
	Sedation	0					
	Sedation (6to<12)	1, 73	1	62	1	11	RR, 0.18; 95% CI, 0.01 to 2.63[20]
	Somnolence	0					
	Hyperprolactinemia	0					
	Prolactin-related events	0					
Aripiprazole	Any AE	1, 69	8	34	12	35	RR, 0.69; 95% CI, 0.32 to 1.47[21]

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
vs. Risperidone	Any AE (6to<12)	1, 114	25	62	39	52	RR, 0.54; 95% CI, 0.38 to 0.76[20]
	AE limiting treatment	2, 272	0 4	34 66	0 6	35 137	Not estimable[21] RR, 1.38; 95% CI, 0.40 to 4.74[18]
	Any EPS	0					
	Akathisia	2, 263	5 0	66 31	7 0	137 29	RR, 1.48; 95% CI, 0.49 to 4.50[18] Not estimable[22]
	Akathesia (6to<12)	1, 114	5	62	3	52	RR, 1.40; 95% CI, 0.35 to 5.57[20]
	Dystonia	1, 59	3	29	1	30	RR, 3.10; 95% CI, 0.34 to 28.15[23]
	Weight (kg)	1, 215	NA	47	NA	168	MD, -0.90; 95% CI, -1.81 to 0.01[18]
	BMI ($kg \cdot m^{-2}$)	1, 215	NA	47	NA	168	MD, -0.25; 95% CI, -0.62 to 0.12[18]
	BMI ($kg \cdot m^{-2}$) (12+)	1, 142	NA	70	NA	72	MD, -0.31; 95% CI, -1.78 to 1.16[24]
	≥7% increase in weight	2, 245	24 0	41 34	87 7	135 35	RR, 0.91; 95% CI, 0.68 to 1.21[18] RR, 0.07; 95% CI, 0.58 to 1.04[21]
	Increased total cholesterol	0					
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	0					
	Increased fasting glucose	0					
	Sedation	1, 56	1	27	0	29	RR, 3.21; 95% CI, 0.14 to 75.68[23]
	Sedation (6to<12)	1, 114	1	62	2	52	RR, 0.42; 95% CI, 0.04 to 4.49[20]
	Somnolence	2, 116	6 8	27 31	5 5	29 29	RR, 1.29; 95% CI, 0.44 to 3.74[23] RR, 1.50; 95% CI, 0.55 to 4.05[22]
	Hyperprolactinemia	0					
	Prolactin-related events	0					
Aripiprazole vs. Ziprasidone	Any AE	0					
	AE limiting treatment	2, 115	2 4	20 66	6 0	14 15	RR, 0.23; 95% CI, 0.05 to 0.99[25] RR, 2.15; 95% CI, 0.12 to 37.92[18]
	Any EPS	1, 34	2	40	0	14	RR, 3.57; 95% CI, 0.18 to 69.14[25]
	Akathisia	1, 81	5	66	0	15	RR, 2.63; 95% CI, 0.15 to 45.11[18]
	Dystonia	0					
	Weight (kg)	0					
	BMI ($kg \cdot m^{-2}$)	0					
	≥7% increase in weight	0					
	Increased total	0					

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
	cholesterol						
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	0					
	Increased fasting glucose	0					
	Sedation	0					
	Somnolence	0					
	Hyperprolactinemia	0					
	Prolactin-related events	0					
Clozapine vs. Olanzapine	Any AE	2, 109	1 12	2 55	15 13	24 28	RR, 0.80; 95% CI, 0.19 to 3.31[26] RR, 0.47; 95% CI, 0.25 to 0.89[27]
	AE limiting treatment	2, 65	0 2	2 18	9 1	24 21	RR, 0.44; 95% CI, 0.03 to 5.78[26] RR, 2.33; 95% CI, 0.23 to 23.66[28]
	AE limiting treatment (12+)	2, 65	1 4	12 28	0 4	13 12	RR, 3.23; 95% CI, 0.14 to 72.46[27] RR, 0.43; 95% CI, 0.13 to 1.44[5]
	Any EPS	0					
	Akathisia	1, 32	1	16	1	16	RR, 1.00; 95% CI, 0.07 to 14.64[29]
	Dystonia	2, 58	0 1	2 16	1 1	24 16	RR, 2.78; 95% CI, 0.14 to 54.04[26] RR, 1.00; 95% CI, 0.07 to 14.64[29]
	Weight (kg)	5, 136	NA	62	NA	74	MD, -1.56; 95% CrI, -5.12 to 1.57[27-31]
	Weight (kg) (6to<12)	1, 23	NA	15	NA	8	MD, -6.70; 95% CI, -14.76 to 1.36[29]
	BMI ($kg \cdot m^{-2}$)	3, 87	NA	40	NA	47	MD, -0.66; 95% CrI, -2.59 to 1.23[27-29]
	BMI ($kg \cdot m^{-2}$) (6to<12)	2, 40	NA NA	15 8	NA NA	8 9	MD, -2.30; 95% CI, -5.42 to 0.82[29] MD, 1.00; 95% CI, -2.67 to 4.67[32]
	≥7% increase in weight	2, 69	5 3	15 18	9 2	15 21	RR, 0.56; 95% CI, 0.24 to 1.27[29] RR, 1.75; 95% CI, 0.33 to 9.34[28]
	≥7% increase in weight (6to<12)	2, 63	9 1	15 28	7 3	8 12	RR, 0.69; 95% CI, 0.42 to 1.12[29] RR, 0.14; 95% CI, 0.02 to 1.24[32]
	Increased total cholesterol	2, 55	2 1	13 12	4 0	17 13	RR, 0.65; 95% CI, 0.14 to 3.04[28] RR, 3.23; 95% CI, 0.23 to 3.55[27]
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	2, 57	10 1	14 12	8 0	18 13	RR, 1.61; 95% CI, 0.87 to 2.97[28] RR, 3.23; 95% CI, 0.14 to 72.46[27]
	Increased fasting glucose	0					

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
	Sedation	1, 26	0	2	0	24	Not estimable[26]
	Sedation (12+)	1, 40	4	28	0	12	RR, 4.03; 95% CI, 0.23 to 69.58[5]
	Somnolence	3, 96	20	46	21	50	RR, 1.09; 95% CrI, 0.41 to 2.75[27-29]
	Hyperprolactinemia	2, 51	0 0	2 15	2 7	24 10	RR, 1.67; 95% CI, 0.10 to 27.14[26] RR, 0.05; 95% CI, 0.00 to 0.72[14]
	Hyperprolactinemia (12+)	1, 40	0	28	2	12	RR, 0.09; 95% CI, 0.00 to 1.74[5]
	Prolactin-related events	1, 25	1	12	0	13	RR, 3.23; 95% CI, 0.14 to 72.46[27]
	Prolactin-related events (12+)	1, 40	0	28	0	12	Not estimable[5]
Clozapine vs. Quetiapine	Any AE	1, 4	1	2	1	2	RR, 1.00; 95% CI, 0.14 to 7.10[26]
	AE limiting treatment	1, 4	0	2	1	2	RR, 0.33; 95% CI, 0.02 to 5.33[26]
	Any EPS	0					
	Akathisia	0					
	Dystonia	1, 4	0	2	0	2	Not estimable[26]
	Weight (kg)	0					
	BMI ($kg \cdot m^{-2}$)	0					
	≥7% increase in weight	0					
	Increased total cholesterol	0					
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	0					
	Increased fasting glucose	0					
	Sedation	1, 4	0	2	0	2	Not estimable[26]
	Somnolence	0					
	Hyperprolactinemia	0					
	Prolactin-related events	0					
Clozapine vs. Risperidone	Any AE	1, 47	1	2	33	45	RR, 0.68; 95% CI, 0.17 to 2.76[26]
	AE limiting treatment	1, 31	0	2	13	29	RR, 0.37; 95% CI, 0.03 to 4.80[26]
	AE limiting treatment (12+)	1, 61	4	28	9	33	RR, 0.52; 95% CI, 0.18 to 1.52[5]
	Any EPS	0					
	Akathisia	1, 35	1	16	0	19	RR, 3.53; 95% CI, 0.15 to 81.11[18]

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
	Dystonia	2, 82	0 1	2 16	1 2	45 19	RR, 5.11; 95% CI, 0.26 to 100.62[26] RR, 0.59; 95% CI, 0.06 to 5.96[29]
	Weight (kg)	2, 89	NA NA	15 7	NA NA	15 52	MD, -0.30; 95% CI, -1.91 to 1.31[29] MD,-1.50: 95% CI, -4.55 to 1.55[30]
	Weight (kg) (6to<12)	1, 25	NA	15	NA	10	MD, 2.30; 95% CI, -3.90 to 8.50[29]
	BMI ($kg \cdot m^{-2}$)	1, 30	NA	15	NA	15	MD, -0.20; 95% CI, -0.77 to 0.37[29]
	BMI ($kg \cdot m^{-2}$) (6to<12)	2, 57	NA NA	15 8	NA NA	10 24	MD, 1.00; 95% CI, -0.95 to 2.85[29] MD, 3.80; 95% CI, 1.37 to 6.23[32]
	≥7% increase in weight	1, 30	5	15	4	15	RR, 1.25; 95% CI, 0.41 to 3.77[29]
	≥7% increase in weight (6to<12)	2, 86	9 1	15 28	6 2	10 33	RR, 1.00; 95% CI, 0.52 to 1.92[29] RR, 0.59; 95% CI, 0.06 to 6.16[32]
	Increased total cholesterol	0					
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	0					
	Increased fasting glucose	0					
	Sedation	1, 47	0	2	3	45	RR, 2.19; 95% CI, 0.14 to 33.36[26]
	Sedation (12+)	1, 61	4	28	1	33	RR, 4.71; 95% CI, 0.56 to 39.78[5]
	Somnolence	1, 35	9	16	6	19	RR, 1.78; 95% CI, 0.81 to 3.93[29]
	Hyperprolactinemia	1, 47	0	2	11	45	RR, 0.67; 95% CI, 0.05 to 8.79[26]
	Hyperprolactinemia (12+)	1, 61	0	28	6	33	RR, 0.09; 95% CI, 0.01 to 1.53[5]
	Prolactin-related events	1, 47	0	2	5	45	RR, 1.39; 95% CI, 0.10 to 19.71[26]
	Prolactin-related events (12+)	1, 61	0	28	1	33	RR, 0.39; 95% CI, 0.02 to 9.23[5]
Olanzapine vs. Quetiapine	Any AE	1, 26	15	24	1	2	RR, 1.25; 95% CI, 0.30 to 5.17[26]
	AE limiting treatment	2, 150	9 1	24 58	1 0	2 66	RR, 0.75; 95% CI, 0.17 to 3.29[26] RR, 3.41; 95% CI, 0.14 to 82.04[18]
	AE limiting treatment (6to<12)	2, 84	0 2	26 18	0 1	24 16	Not estimable[33] RR, 1.78; 95% CI, 0.18 to 17.80[32]
	AE limiting treatment (12+)	1, 34	5	18	1	16	RR, 4.44; 95% CI, 0.58 to 34.14[32]
	Any EPS						
	Akathisia	3, 194	13	94	8	100	RR, 1.65; 95% CrI, 0.42 to 8.06[18, 33, 34]

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
	Akathisia (6to<12)	2, 79	8 0	26 14	6 0	24 15	RR, 1.26; 95% CI, 0.50 to 3.03[33] Not estimable[32]
	Dystonia	1, 26	1	24	0	2	RR, 0.36; 95% CI, 0.02 to 7.00[26]
	Dystonia (6to<12)	1, 29	0	14	0	15	Not estimable[32]
	Weight (kg)	3, 232	NA	116	NA	116	MD, 4.00; 95% CrI, -1.67 to 10.79[18, 35, 36]
	Weight (kg) (6to<12)	3, 185	NA	90	NA	95	MD, 7.91; 95% CrI, 3.65 to 12.29[33, 35, 36]
	BMI ($kg \cdot m^{-2}$)	3, 232	NA	116	NA	116	MD, 1.36; 95% CrI, -0.29 to 3.40[18, 35, 36]
	BMI ($kg \cdot m^{-2}$) (6to<12)	4, 203	NA	99	NA	104	MD, 2.68; 95% CrI, 0.96 to 4.27[32, 33, 35, 36]
	≥7% increase in weight	3, 192	72	99	47	93	RR, 1.41; 95% CrI, 0.65 to 2.83[18, 34, 35]
	≥7% increase in weight (6to<12)	1, 91	18	44	22	47	RR, 0.87; 95% CI, 0.55 to 1.40[35]
	Increased total cholesterol	1, 33	0	13	1	20	RR, 0.5 ; 95% CI, 0.02 to 11.42[37]
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	1, 33	1	13	1	20	RR, 1.54: 95% CI, 0.11 to 22.49[37]
	Increased fasting glucose	0					
	Sedation	2, 46	0 3	24 10	0 1	2 10	Not estimable[26] RR, 3.00; 95% CI, 0.37 to 24.17[34]
	Sedation (6to<12)	1, 50	12	26	11	24	RR, 1.01; 95% CI, 0.55 to 1.84[33]
	Somnolence	0					
	Hyperprolactinemia	2, 45	2 5	24 13	0 1	2 6	RR, 0.60; 95% CI, 0.04 to 9.77[26] RR, 2.31; 95% CI, 0.34 to 15.69[38]
	Hyperprolactinemia (12+)	1, 28	3	12	2	16	RR, 2.00; 95% CI, 0.39 to 10.16[37]
	Prolactin-related events	1, 19	3	13	2	6	RR, 0.69; 95% CI, 0.15 to 3.12[38]
	Prolactin-related events (6to<12)	1, 50	0	26	0	24	Not estimable[33]
Olanzapine vs. Risperidone	Any AE	3, 199	50	73	97	126	RR, 0.87; 95% CrI, 0.49 to 1.55[1, 26, 39]
	Any AE (6to<12)	1, 34	13	13	15	21	RR, 1.37; 95% CI, 1.03 to 1.83[1]
	AE limiting treatment	6, 436 (1 Study n=36 no events)	16	164	30	272	RR, 0.87; 95% CrI, 0.21 to 2.18[1, 3, 4, 18, 26, 40]
	AE limiting treatment	1, 69	2	18	5	51	RR, 1.13; 95% CI, 0.24 to 5.34[32]

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
	(6to<12)						
	AE limiting treatment (12+)	3, 148	12	43	23	105	RR, 1.23; 95% CrI, 0.36 to 4.09[1, 5, 32]
	Any EPS	3, 115	13	45	19	70	RR, 0.94; 95% CrI, 0.30 to 2.82[4, 39, 40]
	Akathisia	9, 507	20	192	24	315	RR, 1.17; 95% CrI, 0.59 to 2.40[1, 3, 4, 18, 29, 34, 39-41]
	Akathisia (6to<12)	1, 45	0	14	4	31	RR, 0.24; 95%CI, 0.01 to 4.13[32]
	Dystonia	5, 270	10	108	13	162	RR, 1.65; 95% CrI, 0.44 to 6.07[1, 3, 4, 26, 29, 39]
	Dystonia (6to<12)	1, 45	0	14	1	31	RR, 0.71; 95% CI, 0.03 to 16.45[32]
	Weight (kg)	13, 936	NA	331	NA	605	MD, 2.18; 95% CrI, 1.13 to 3.25[1, 3, 4, 18, 29, 30, 35, 36, 40-44]
	Weight (kg) (6to<12)	4, 295	NA	85	NA	210	MD, 4.40; 95% CrI, -0.54 to 9.86[1, 33, 35, 36]
	BMI ($kg \cdot m^{-2}$)	9, 737	NA	244	NA	493	MD, 0.94; 95% CrI, 0.64 to 1.30[1, 3, 4, 18, 29, 35, 36, 44, 45]
	BMI ($kg \cdot m^{-2}$) (6to<12)	5, 328	NA	94	NA	234	MD, 1.66; 95% CrI, 0.19 to 3.42[1, 32, 33, 35, 36]
	≥7% increase in weight	6, 504	107	150	188	354	RR, 1.36; 95% CrI, 0.93 to 2.04[4, 18, 29, 34, 35, 41]
	≥7% increase in weight (6to<12)	3, 264	28	64	64	200	RR, 1.44; 95% CrI, 0.55 to 5.50}[5, 29, 35]
	Increased total cholesterol	1, 34	0	13	1	21	RR, 0.52; 95% CI, 0.02 to 11.98[37]
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	1, 34	1	13	5	21	RR, 0.32; 95% CI, 0.04 to 2.47[37]
	Increased fasting glucose	1, 49	0	25	0	24	Not estimable[45]
	Sedation	7, 321	35	133	36	188	RR, 1.19; 95% CrI, 0.68 to 2.35[1, 3, 4, 26, 34, 39, 42]
	Sedation (6to<12)	1, 34	3	13	2	21	RR, 2.42; 95% CI, 0.47 to 12.62[1]
	Sedation (12+)	1, 45	0	12	1	33	RR, 0.87; 95% CI, 0.04 to 20.06[5]
	Somnolence	2, 66	9 3	16 12	6 13	19 19	RR, 1.78; 95% CI, 0.81 to 3.93[29] RR, 0.37; 95% CI, 0.13 to 1.02[41]
	Hyperprolactinemia	3, 128	7	49	27	79	RR, 0.46; 95% CrI, 0.11 to 1.70[26, 38, 40]
	Hyperprolactinemia (12+)	2, 75	3 2	12 12	9 6	18 33	RR, 0.50; 95% CI, 0.17 to 1.48[37] RR, 0.92; 95% CI, 0.21 to 3.94[5]
	Prolactin-related events	5, 221	7	84	16	137	RR, 0.78; 95% CrI, 0.24 to 2.35[3, 26, 38, 41, 46]
	Prolactin-related events (6to<12)	1, 34	3	13	2	21	RR, 2.42; 95% CI, 0.47 to 12.62[1]

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
	Prolactin-related events (12+)	1, 45	0	12	1	33	RR, 0.87; 95% CI, 0.04 to 20.06[5]
Olanzapine vs. Ziprasidone	Any AE	0					
	AE limiting treatment	1, 73	1	58	0	15	RR, 0.81; 95% CI, 0.03 to 19.03[18]
	Any EPS						
	Akathisia	1, 73	3	58	0	15	RR, 1.90; 95% CI, 0.10 to 34.89)[18]
	Dystonia	0					
	Weight (kg)	0					
	BMI ($kg \cdot m^{-2}$)	0					
	≥7% increase in weight	0					
	Increased total cholesterol	0					
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	0					
	Increased fasting glucose	0					
	Sedation	0					
	Somnolence	0					
	Hyperprolactinemia	0					
	Prolactin-related events	0					
Quetiapine vs. Risperidone	Any AE	1, 47	1	2	33	45	RR, 0.68; 95% CI, 0.17 to 2.76[26]
	Any AE (6to<12)	1, 63	10	11	39	52	RR, 1.21; 95% CI, 0.95 to 1.55[20]
	AE limiting treatment	2, 250	1 0	2 66	13 6	45 137	RR, 1.73; 95% CI, 0.40 to 7.45[26] RR, 0.16; 95% CI, 0.01 to 2.77[18]
	AE limiting treatment (6to<12)	1, 67	1	16	5	51	RR, 0.64; 95% CI, 0.08 to 5.06[32]
	AE limiting treatment (12+)	1, 67	1	16	7	51	RR, 0.46; 95% CI, 0.06 to 3.43[32]
	Any EPS	1, 22	0	12	0	10	Not estimable[47]
	Akathisia	2, 223	1 1	66 10	7 4	137 10	RR, 0.30; 95% CI, 0.04 to 2.36[18] RR, 0.25; 95% CI, 0.03 to 1.86[34]
	Akathisia (6to<12)	2, 109	1 0	11 15	3 4	52 31	RR, 1.58; 95% CI, 0.18 to 13.77[20] RR, 0.22; 95% CI, 0.01 to 3.88[32]
	Dystonia	1, 47	0	2	1	45	RR, 5.11; 95% CI, 0.26 to 100.62[26]
	Dystonia (6to<12)	1, 46	0	15	1	31	RR, 0.67; 95% CI, 0.03 to 15.46[32]

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
	Weight (kg)	3, 463	NA	116	NA	347	MD, 0.08; 95% CrI, -3.77 to 3.14[18, 35, 36]
	Weight (kg) (6to<12)	2, 250	NA NA	47 24	NA	157 22	MD, -0.81; 95% CI, -3.96 to 2.34[35] MD, -2.50; 95% CI, -5.88 to 0.88[36]
	BMI ($kg \cdot m^{-2}$)	3, 463	NA	116	NA	347	MD, 0.04; 95% CrI, -1.34 to 1.20[18, 35, 36]
	BMI ($kg \cdot m^{-2}$) (6to<12)	3, 283	NA	80	NA	203	MD, -0.27; 95% CrI, -2.28 to 2.30[32, 35, 36]
	≥7% increase in weight	4, 417	55	104	176	313	RR, 0.91; 95% CrI, 0.56 to 1.44[18, 34, 35, 48]
	≥7% increase in weight (6to<12)	1, 204	22	47	56	157	RR, 1.31; 95% CI, 0.91 to 1.90[35]
	Increased total cholesterol	1, 41	1	20	1	21	RR, 1.05; 95% CI, 0.07 to 15.68[37]
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	1, 41	1	20	5	21	RR, 0.21; 95% CI, 0.03 to 1.64[37]
	Increased fasting glucose	0					
	Sedation	3, 89	8	23	12	66	RR, 0.98; 95% CrI, 0.22 to 4.28[26, 34, 48]
	Sedation (6to<12)	1, 63	1	11	2	52	RR, 2.36; 95% CI, 0.23 to 23.83[20]
	Somnolence	1, 22	3	12	1	10	RR, 2.50; 95% CI, 0.31 to 20.45[47]
	Hyperprolactinemia	4, 118	4	31	45	87	RR, 0.20; 95% CrI, 0.06 to 0.73[26, 38, 47, 48]
	Hyperprolactinemia (12+)	1, 34	2	16	9	18	RR, 0.25; 95% CI, 0.06 to 0.99[37]
	Prolactin-related events	2, 74	0 2	2 6	5 5	45 21	RR, 1.39; 95% CI, 0.10 to 19.71[26] RR, 1.40; 95% CI, 0.36 to 5.49[38]
Quetiapine vs. Ziprasidone	Any AE	0					
	AE limiting treatment	1, 81	0	66	0	15	Not estimable[18]
	Any EPS	0					
	Akathisia	1, 81	1	66	0	15	RR, 0.72; 95% CI, 0.03 to 16.78[18]
	Dystonia	0					
	Weight (kg)	0					
	BMI ($kg \cdot m^{-2}$)	0					
	≥7% increase in weight	0					
	Increased total cholesterol	0					
	Increased LDL	0					
	Decreased HDL	0					
	Increased	0					

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
	triglycerides						
	Increased fasting glucose	0					
	Sedation	0					
	Somnolence	0					
	Hyperprolactinemia	0					
	Prolactin-related events	0					
Risperidone vs. Ziprasidone	Any AE	0					
	AE limiting treatment	1, 152	6	137	0	15	RR, 1.51; 95% CI, 0.09 to 25.53[18]
	Any EPS						
	Akathisia	1, 152	7	137	0	15	RR, 1.74; 95% CI, 0.10 to 29.05[18]
	Dystonia	0					
	Weight (kg)	0					
	BMI ($kg \cdot m^{-2}$)	0					
	≥7% increase in weight	0					
	Increased total cholesterol	0					
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	0					
	Increased fasting glucose	0					
	Sedation	0					
	Somnolence	0					
	Hyperprolactinemia	0					
	Prolactin-related events	0					

AE = adverse event; BMI = body mass index; CI = confidence interval; EPS = extrapyramidal symptoms; G1 = group 1; G2 = group 2; HDL = high density lipoprotein; LDL = low density lipoprotein; MD = mean difference; N = number; NA = not applicable; RR = risk ratio; SGA = second generation antipsychotic

Table G5. Findings for GAE: Dose Comparisons - Aripiprazole

Outcome	Author, Year	Low Dose		Medium Dose		High dose (1)		High dose (2)		High dose (3)		High dose (4)	
	Findling 2008a(1)[49] Findling 2008b(2)[50] Findling 2009(3)[51] Marcus 2009(4)[52]	5 mg/day		10 mg/day 10 mg/day 10 mg/day		15 mg/day		20 mg/day		25 mg/day		30mg/day 30mg/day 30 mg/day	
		Count	N	Count	N	Count	N	Count	N	Count	N	Count	N
Any AE	2 3 4	- - 45	- - 52	- 72 53	- 98 59	- - 45	- - 54	8 - -	8 - -	7 - -	7 - -	6 75 -	6 99 -
AE limiting treatment	1 2 3 3 (6to<12) 4	- - - - 5	- - - - 52	7 - 4 3 8	100 - 98 75 59	- - - - 4	- - - - 54	- 0 - - -	- 8 - - -	- 1 - - -	- 7 - - -	4 0 7 11 -	102 6 99 71 -
≥7% increase in weight	1 3 4	- - 17	- - 52	11 4 9	99 98 59	- - 16	- - 54	- - -	- - -	- - -	- - -	9 12 -	97 99 -
High cholesterol	3 3 (6to<12) 4	- - 0	- - 52	27 30 0	64 73 59	- - 0	- - 54	- - -	- - -	- - -	- - -	28 34 -	65 68 -
High LDL	4	0	52	0	59	0	54	-	-	-	-	-	-
Low HDL	3 3 (6to<12) 4	- - 1	- - 52	10 13 0	65 73 59	- - 2	- - 54	- - -	- - -	- - -	- - -	9 6 -	65 67 -
High triglycerides	3 3 (6to<12) 4	- - 6	- - 52	22 21 6	65 73 59	- - 2	- - 54	- - -	- - -	- - -	- - -	22 28 -	65 67 -
High fasting glucose	1 3 3 (6to<12) 4	- - - 6	- - - 52	2 1 0 6	86 65 73 59	- - - 1	- - - 54	- - - -	- - - -	- - - -	- - - -	0 2 2 -	79 64 67 -
Prolactin-related events	3 (6to<12)	-	-	3	75	-	-	-	-	-	-	0	71
Any EPS	3 3 (6to<12) 4	- - 12	- - 52	23 3 13	98 75 59	- - 12	- - 54	- - -	- - -	- - -	- - -	39 2 -	99 71 -
Akathisia	1 3	- -	- -	5 8	100 98	- -	- -	- -	- -	- -	- -	12 11	102 99

Outcome	Author, Year	Low Dose		Medium Dose		High dose (1)		High dose (2)		High dose (3)		High dose (4)	
	3 (6to<12) 4	- 1	- 52	1 2	75 59	- 0	- 54	- -	- -	- -	- -	2 -	71 -
Dystonia	1 2 3 3 (6to<12)	- - - -	- - - -	4 - 0 2	100 - 98 75	- - - -	- - - -	- 1 - -	- 8 - -	- 1 - -	- 7 - -	2 0 5 1	102 6 99 71
Somnolence	1 2 3 3 (6to<12) 4	- - - - 4	- - - - 52	11 - 19 5 5	100 - 98 75 59	- 1 - - 5	- 8 - - 54	- 0 - - -	- 7 - - -	- 1 - - -	- 6 - - -	22 - 27 1 -	102 - 99 71 -
Sedation	2 3 4	- - 9	- - 52	- 2 17	- 98 59	- - 13	- - 54	0 - -	8 - -	0 - -	7 - -	1 0 -	6 99 -
		Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N
BMI ($kg \cdot m^{-2}$)	1 3 4	- - 0.6 (0.2)	- - 52	0.0(0.8) 0.2(0.8) 0.6(0.2)	99 75 59	- - 0.8 (0.2)	- - 59	- - -	- - -	- - -	- - -	0.0(0.8 0.3(1.1) -	97 72 -
Weight (kg)	1 2 3 3 (6to<12) 4	- - - - 1.3 (2.2)	- - - - 53	0.0(2.1) - 0.8(1.7) 6.5(NR) 1.3	100 - 75 75 59	- - - - 1.5(2.2)	- - - - 54	- -0.2(2.5) - - -	- 8 - - -	- 0.9(2.3) - - -	- 7 - - -	0.2(2.3) 0.4(1.8) 1.1(2.3) 6.6(NR) -	102 6 73 71 -

AE = adverse event; BMI = body mass index; EPS = extrapyramidal symptoms; HDL = high density lipoprotein; LDL = low density lipoprotein; N = number

Table G6. Findings for GAE: Dose Comparisons - Asenapine

Outcome	Author, Year	Low Dose		Medium Dose		High dose	
	Findling 2015a(1)[53] Findling 2015b(2)[54]	5 mg/day 5 mg/day		10 mg/day 10 mg/day		20 mg/day	
		Count	N	Count	N	Count	N
Any AE	1 2	61 78	98 104	71 72	106 99	- 85	- 99
AE limiting treatment	1 2	6 7	98 104	8 3	106 99	- 5	- 99
≥7% increase in weight	1 2	9 11	95 92	10 8	99 90	- 7	- 87
Hyperprolactinemia	1	23	98	20	106	-	-
Any EPS	1 2	5 4	98 104	11 4	106 99	- 5	- 99
Akathisia	1 2	4 2	98 104	7 2	106 99	- 1	- 99
Somnolence	1 2	24 49	98 104	31 52	106 99	- 48	- 99
Metabolic syndrome	1	1	98	2	106	-	-
		Mean (SD)	N	Mean (SD)	N	Mean (SD)	N
BMI ($kg \cdot m^{-2}$)	2	0.60(0.79)	104	0.57(0.89)	99	0.49(0.81)	99
Weight (kg)	1	0.09(0.21)	95	0.06(0.20)	99	-	-

AE = adverse event; BMI = body mass index; EPS = extrapyramidal symptoms; N = number

Table G7. Findings for GAE: Dose Comparisons - Paliperidone

Outcome	Author, Year	Low Dose		Medium Dose		High dose (1)		High dose (2)	
	Johnson 2011(1)[56] Singh 2011(2)[57]	1.5 mg/day		6 mg/day 3/6 mg/day		9 mg/day		12 mg/day 6/12 mg/day	
		Count	N	Count	N	Count	N	Count	N
Any AE	1 2	 27	 54	3 32	8 48	6	9	6 36	8 48
AE limiting treatment	1 2	 1	 54	0 1	8 48	0	9	0 1	8 48
≥7% increase in weight	2	3	54	6	48	-	-	6	47
Hyperprolactinemia	1	-	-	4	8	6	9	3	8
Prolactin-related events	1 2	 0	 54	0 2	8 48	0	9	0 0	8 48
Akathisia	2	2	54	4	48	-	-	7	47
Dystonia	2	1	54	1	48	-	-	4	47
Somnolence	2	3	54	7	48	-	-	10	48
		Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N
Weight (kg)	2	0.3(1.52)	54	1.1(2.13)	48	-	-	1.4(2.16)	48

AE = adverse event; N = number

Table G8. Findings for GAE: Dose Comparisons - Quetiapine

Outcome	Author, Year	Low Dose		Medium Dose		High dose (1)		High dose (2)	
	Berger 2008(1)[58] Findling 2012a(2)[59] Pathak 2013(3)[60]	200 mg/day		400 mg/day 400 mg/day 400 mg/day		600 mg/day		800 mg/day	
		Count	N	Count	N	Count	N	Count	N
Any AE	1 2	1 -	46 -	3 58	45 73	- -	- -	- 55	- 74
AE limiting treatment	2 3	- -	- -	5 15	73 95	- 7	- 98	7 -	74 -
≥7% increase in weight	2 3	- -	- -	17 14	73 95	- 10	- 98	14 -	74 -
High cholesterol	3	- -	- -	15 -	55 -	15 -	54 -	- -	- -
High LDL	3	-	-	0	90	1	85	-	-
Low HDL	3	-	-	2	77	13	77	-	-
High Triglycerides	3	-	-	14	76	15	73	-	-
High fasting glucose	3	-	-	1	86	1	81	-	-
Hyperprolactinemia	2 3	- -	- -	1 12	40 76	- 10	- 81	3 -	36 -
Any EPS	2 3	9 4	73 95	- 3	- 98	10 -	74 -		
Somnolence	2 3	- -	- -	20 27	73 95	- 31	- 98	22 -	74 -
Sedation	2 3	- -	- -	4 22	73 95	- 25	- 98	4 -	74 -
		Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N
Weight (kg)	1 2	- -	- -	2.2(2.6) 1.7(1.98)	73 95	- 1.7(2.34)	- 98	1.8(2.8) -	74 -

AE = adverse event; EPS = extrapyramidal symptoms; HDL = high density lipoprotein; LDL = low density lipoprotein; N = number

Table G9. Findings for GAE: Dose Comparisons - Risperidone

Outcome	Author, Year	Low Dose		Medium Dose		High dose (1)		High dose (2)	
	Haas 2009a(1)[61] Haas 2009b(2)[62] Haas 2009c(3)[63] Kent 2013(4)[64]	0.15-0.6 mg/day 0.125/0.175 mg/day		 1-3 mg/day 0.5-2.5 mg/day 1.25/1.75 mg/day		1.5-6 mg/day		 4-6 mg/day 3-6 mg/day	
		Count	N	Count	N	Count	N	Count	N
Any AE	1 2 3 4	86 - - 18	132 - - 30	- 41 45 27	- 55 50 31	93 - - -	125 - - -	- 39 58 -	- 51 61 -
AE limiting treatment	1 2 3 4	6 - - 0	132 - - 30	- 3 3 1	- 55 50 31	5 - - -	125 - - -	- 4 10 -	- 51 61 -
≥7% increase in weight	3	-	-	7	50	-	-	6	61
Hyperprolactinemia	1	55	132	-	-	70	125	-	-
Prolactin-related events	1 2 3 4	2 - - 0	132 - - 30	- 0 2 1	- 55 50 31	7 - - -	125 - - -	- 0 3 -	- 51 61 -
Any EPS	1 2 3	13 - -	132 -	- 18 4	- 55 50	41 - -	125 - -	- 20 15	- 51 61
Akathisia	1	2	132	-	-	11	125	-	-
Dystonia	1	8	132	-	-	23	125	-	-
Somnolence	2 3 4	- - 0	- - 30	13 21 7	55 50 31	- - -	- - -	6 34 -	51 61 -
Sedation	3 4	- 1	- 30	10 8	50 31	- -	- -	13 -	61 -
		Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N
BMI ($kg \cdot m^{-2}$)	2 3 4	- - 0.4(0.7)	- - 30	0.36(NR) 0.7(0.9) 1.1(1.35)	55 50 31	- - -	- - -	0.48(NR) 0.5(0.9) -	51 61 -
Weight (kg)	1 2 3 4	1.7 - - 1.2	132 - - 30	- 1.3(NR) 1.9(1.7) 2.4(2.07)	- 55 50 31	3.2(3.49) - - -	125 - - -	- 1.5(NR) 1.4(2.4) -	- 51 61 -

AE = adverse event; BMI = body mass index; EPS = extrapyramidal symptoms; N = number

Table G10. Findings for GAE: Dose Comparisons - Ziprasidone

Outcome	Author, Year	Low Dose		High Dose	
	Delbello 2008(1)[65]	80 mg/day		160 mg/day	
		Count	N	Count	N
Any AE	1	21	23	38	40
AE limiting treatment	1	3	23	16	40
≥7% increase in weight	1	3	23	1	40
High fasting glucose	1	0	23	0	40
Akathisia	1	1	23	3	40
Dystonia	1	1	23	3	40
Somnolence	1	5	23	15	40
Sedation	1	5	23	15	40

AE = adverse event; N = number

Table G11. Findings for GAE: FGA versus Placebo

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
FGA vs. placebo	Any AE	0					
	AE limiting treatment	3, 153	22	77	11	76	RR, 2.43; 95% CrI, 0.47 to 23.08[17, 66]
	Any EPS	0					
	Akathisia	0					
	Dystonia, see haloperidol	1, 66					
	Dystonia (12+), see haloperidol	1, 66					
	Weight (kg), see various FGA's	2, 40					
	BMI ($kg \cdot m^{-2}$)	0					
	≥7% increase in weight	0					
	Increased total cholesterol, see various FGA's	1, 40					
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides, see various FGA's	1, 40					
	Increased fasting glucose, see various FGA's	1, 40					
	Sedation	0					
	Somnolence, see haloperidol	1, 72					
	Hyperprolactinemia	0					
	Prolactin-related events	0					
Haloperidol vs. placebo	Any AE	0					
	AE limiting treatment	2, 109	10 9	33 22	11 0	32 22	RR, 0.88; 95% CI, 0.44 to 1.78[66] RR, 19.00; 95% CI, 1.17 to 307.63[17]
	Any EPS	0					
	Akathisia	0					
	Dystonia	1, 66	1	33	0	33	RR, 3.00; 95% CI, 0.13 to 71.07[66]
	Dystonia (12+)	1, 66	9	33	0	33	RR, 19.00; 95% CI, 1.15 to 313.64[67]
	Weight (kg)	0					

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
	BMI ($kg \cdot m^{-2}$)	0					
	≥7% increase in weight	0					
	Increased total cholesterol	0					
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	0					
	Increased fasting glucose	0					
	Sedation	0					
	Somnolence	1, 72	5	36	0	36	RR, 11.00; 95% CI, 0.63 to 191.88[66]
	Hyperprolactinemia	0					
	Prolactin-related events	0					
Pimozide vs. placebo	Any AE	0					
	AE limiting treatment	1, 44	3	22	0	22	RR, 7.00; 95% CI, 0.38 to 128.02[17]
	Any EPS	0					
	Akathisia	0					
	Dystonia	0					
	Weight (kg)	0					
	BMI ($kg \cdot m^{-2}$)	0					
	≥7% increase in weight	0					
	Increased total cholesterol	0					
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	0					
	Increased fasting glucose	0					
	Sedation	0					
	Somnolence	0					
	Hyperprolactinemia	0					
	Prolactin-related events	0					
Various	Any AE	0					

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
FGA's vs. placebo	AE limiting treatment	0					
	Any EPS	0					
	Akathisia	0					
	Dystonia	0					
	Weight (kg)	1, 40	NA	16	NA	24	MD, 0.87; 95% CI, -1.58 to 3.32[11]
	BMI ($kg \cdot m^{-2}$)	0					
	≥7% increase in weight	0					
	Increased total cholesterol	1, 40	1	16	0	24	RR, 4.41; 95% CI, 0.19 to 102.00[11]
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	1, 40	3	16	1	24	RR, 4.50; 95% CI, 0.51 to 39.53[11]
	Increased fasting glucose	1, 40	0	16	0	24	Not estimable[11]
	Sedation	0					
	Somnolence	0					
	Hyperprolactinemia	0					
	Prolactin-related events	0					

AE = adverse event; BMI = body mass index; CI = confidence interval; EPS = extrapyramidal symptoms;FGA = first generation antipsychotic; G1 = group 1; G2 = group 2; HDL = high density lipoprotein; LDL = low density lipoprotein; MD = mean difference; N = number; NA = not applicable; RR = risk ratio

Table G12. Findings for GAE: SGA versus Placebo

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
SGA vs. placebo	Any AE	26, 3518	1375	2232	679	1286	RR, 1.25; 95% CrI, 1.16 to 1.36[1-26]
	Any AE (6to<12) see risperidone	1, 335					
	Any AE (12+)	2, 233	10 41	43 98	13 25	44 48	RR, 0.79; 95% CI, 0.39 to 1.60[27] RR, 0.80; 95% CI, 0.56 to 1.15[28]
	AE limiting treatment	23, 3894 5, 348	179	2544	60	135	RR, 1.58; 95% CrI, 1.13 to 2.28 [2, 4-6, 8, 9, 11, 14, 17, 19, 21, 23-26, 29-31] Not estimable[1, 15, 18, 32, 33]
	AE limiting treatment (6to<12)	3, 584	14 2 0	146 172 19	0 1 0	64 163 20	RR, 12.82; 95% CI, 0.78 to 211.72[5] RR, 1.90; 95% CI, 0.17 to 20.70[34] Not estimable[35]
	AE limiting treatment (12+)	3, 266	0 1 1	30 98 31	0 1 1	30 48 29	Not estimable[36] RR, 0.49; 95% CI, 0.03 to 7.66[28] RR, 0.94; 95% CI, 0.06 to 14.27[37]
	Any EPS	15, 2730 2, 32	233	1757	40	973	RR, 2.94; 95% CI, 2.02 to 4.27[1, 2, 5, 7, 9, 13, 14 {Snyder, 2002 #116, 20, 21, 23, 25, 29, 38, 39] Not estimable[31, 40]
	Any EPS (6to<12)	2, 629	62 3	197 172	7 1	97 163	RR, 4.36; 95% CI, 2.08 to 9.17[5] RR, 2.84; 95% CI, 0.30 to 27.06[34]
	Akathisia	20, 3489	145	2333	56	1156	RR, 1.24; 95% CrI, 0.78 to 2.19[2, 4, 5, 7-9, 11, 16, 19, 21, 23-26, 29, 30, 38, 41-43]
	Akathisia (6to<12)	2, 629	20 0	197 172	2 0	97 163	RR, 4.92; 95% CI, 1.17 to 20.64[5] Not estimable[34]
	Dystonia	6, 1497 4, 194	21	1032	4	465	RR, 1.65; 95% CrI, 0.44 to 6.07[5, 7, 8, 11, 24, 29] Not estimable[14, 16, 17, 44]
	Dystonia (6to<12)	3, 652	7 2 0	197 172 11	2 1 0	97 163 12	RR, 1.72; 95% CI, 0.36 to 8.14[5] RR, 1.90; 95% CI, 0.17 to 20.70[34] Not estimable[44]
	Weight (kg)	36, 3759	NA	2284	NA	1486	MD, 1.51; 95% CI, 1.08 to 1.97[1, 2, 4, 5, 7, 10-22, 24-26, 29, 30, 32, 33, 37-40, 42, 43, 45-49]
	Weight (kg) (6to<12), see risperidone	4, 467					
	Weight (kg) (12+)	2, 119	NA NA	30 30	NA NA	30 29	MD, 2.19; 95% CI, 0.73 to 3.65[36] MD, 8.49; 95% CI, 4.90 to 12.08[37]
	BMI ($kg \cdot m^{-2}$)	15, 2313	NA	1482	NA	831	MD, 0.65; 95% CI, 0.42 to 0.89[2, 4, 5, 7, 8, 15, 18, 19, 21, 29, 30, 34, 40, 42, 48]
	BMI ($kg \cdot m^{-2}$) (6to<12), see risperidone	2, 405					
	≥7% increase in weight	17, 3057	337	2023	42	1034	RR, 3.53; 95% CrI, 2.49 to 5.23[1, 2, 4, 5, 8-13, 21, 22, 29, 30, 37, 39, 42]

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
	≥7% increase in weight (6to<12), see risperidone	1, 70					
	Increased total cholesterol	6, 643 2, 218	92	410	13	233	RR, 3.17; 95% CI, 1.29 to 9.13[4, 5, 30, 39, 40, 49] Not estimable[2, 37]
	Increased total cholesterol (6to<12), see aripiprazole	1, 198					
	Increased LDL	3, 384 2, 294	4	239	0	145	RR, 2.71; 95% CrI, 0.32 to 23.42[4, 39, 40] Not estimable[2, 30]
	Decreased HDL	6, 839	46	564	24	275	RR, 0.95; 95% CrI, 0.48 to 2.04[2, 4, 5, 30, 39, 40]
	Decreased HDL (6to<12), see aripiprazole	1, 197					
	Increased triglycerides	10, 1383	130	897	38	486	RR, 1.64; 95% CrI, 1.09 to 2.63[2, 4, 5, 13, 30, 39, 40, 42, 46, 49]
	Increased triglycerides (6to<12), see aripiprazole	1, 197					
	Increased fasting glucose	7, 1204 2, 154	10	797	5	407	RR, 0.85; 95% CrI, 0.26 to 2.76[2, 5, 29, 30, 39, 40, 46] Not estimable[4, 49]
	Increased fasting glucose (6to<12), see aripiprazole	1, 197					
	Sedation	20, 2561	284	1596	78	965	RR, 2.19; 95% CrI, 1.50 to 3.41[2, 4, 5, 7, 9, 10, 12, 13, 17, 19, 21, 24, 26, 32, 39, 40, 42, 43, 46, 50]
	Sedation (6to<12) see risperidone	1, 23					
	Sedation (12+), see aripiprazole	1, 60					
	Somnolence	25, 3793	548	2381	117	1412	RR, 2.92; 95% CrI, 2.27 to 3.91[2, 4, 5, 7, 9, 11-16, 18-21, 23-26, 29, 33, 37-39, 42]
	Somnolence (6to<12)	2, 545	3 6	172 146	2 0	163 64	RR, 1.42; 95% CI, 0.24 to 8.40[34] RR, 5.75; 95% CI, 0.33 to 100.53[5]
	Somnolence (12+), see aripiprazole	1, 146					
	Hyperprolactinemia	12, 2009	231	1261	98	748	RR, 2.04; 95% CrI, 0.82 to 5.44[4, 9, 13, 18, 24, 26, 29, 30, 32, 39, 42, 46]
	Prolactin-related events	6, 783 5, 457	11	506	3	277	RR, 1.47; 95% CrI, 0.41 to 5.37[5, 11, 18, 19, 21, 26] Not estimable[14, 16, 23, 33, 47]

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
	Prolactin-related events (6to<12)	2, 545	3 5	146 172	2 0	64 163	RR, 0.66; 95% CI, 0.11 to 3.84[5] RR, 10.43; 95% CI, 0.58 to 187.10[34]
Aripiprazole vs. placebo	Any AE	7, 840	266	531	123	309	RR, 1.26; 95% CrI, 0.88 to 2.06[1-7]
	Any AE (12+)	1, 146	41	98	25	48	RR, 0.80; 95% CI, 0.56 to 1.15[28]
	AE limiting treatment	5, 969 1, 82	46	680	12	371	RR, 1.91; 95% CrI, 0.82 to 4.65[2, 4-6, 29] Not estimable[1]
	AE limiting treatment (6to<12)	1, 210	14	146	0	64	RR, 12.82; 95% CI, 0.78 to 211.72[5]
	AE limiting treatment (12+)	2, 206	0 1	30 98	0 1	30 48	Not estimable[36] RR, 0.49; 95% CI, 0.03 to 7.66[28]
	Any EPS	6, 1000	117	655	17	345	RR, 3.10; 95% CrI, 1.26 to 7.01[1, 2, 5, 7, 29, 38]
	Any EPS (6to<12)	1, 294	62	197	7	97	RR, 4.36; 95% CI, 2.08 to 9.17[5]
	Akathisia	7, 1325	48	873	23	452	RR, 0.86; 95% CrI, 0.31 to 2.14[2, 4, 5, 7, 29, 38, 41]
	Akathisia (6to<12)	1, 294	20	197	2	97	RR, 4.92; 95% CI, 1.17 to 20.64[5]
	Dystonia	3, 656	13	431	4	225	RR, 1.42; 95% CrI, 0.21 to 8.90 [5, 7, 29]
	Dystonia (6to<12)	1, 294	7	197	2	97	RR, 1.72; 95% CI, 0.36 to 8.14[5]
	Weight (kg)	7, 1042	NA	647	NA	395	MD, 0.98; 95% CrI, 0.54 to 1.48[1, 2, 4, 5, 7, 29, 38]
	Weight (kg) (12+)	1, 60	NA	30	NA	30	MD, 2.19; 95% CI, 0.73 to 3.65[36]
	BMI ($kg \cdot m^{-2}$)	5, 881	NA	587	NA	294	MD, 0.33; 95% CI, 0.07 to 0.67[2, 4, 5, 7, 29]
	≥7% increase in weight	5, 991	93	647	15	344	RR, 3.01; 95% CrI, 1.33 to 7.10[1, 2, 4, 5, 29]
	Increased total cholesterol	3, 511	0 1 55	52 47 130	0 0 11	166 51 65	Not estimable[2] RR, 3.25; 95% CI, 0.14 to 77.88 [4] RR, 2.50; 95% CI, 1.41 to 4.44[5]
	Increased total cholesterol (6to<12)	1, 198	64	141	15	57	RR, 1.72; 95% CI, 1.08 to 2.76[5]
	Increased LDL	2, 316	0 1	52 47	0 0	166 51	Not estimable[2] RR, 3.25; 95% CI, 0.14 to 77.88[4]
	Decreased HDL	3, 509	22	342	13	167	RR, 0.82; 95% CrI, 0.17 to 4.20[2, 4, 5]
	Decreased HDL (6to<12)	1, 197	19	140	13	57	RR, 0.60; 95% CI, 0.32 to 1.12[5]
	Increased triglycerides	3, 509	64	342	22	167	RR, 1.51; 95% CrI, 0.53 to 4.65[2, 4, 5]
	Increased triglycerides (6to<12)	1, 197	49	140	21	57	RR, 0.95; 95% CI, 0.63 to 1.43[5]
	Increased fasting glucose	3, 651 1, 98	7	459	3	192	RR, 0.90; 95% CrI, 0.16 to 5.44[2, 5, 29] Not estimable[4]
	Increased fasting glucose (6to<12)	1, 197	2	140	1	57	RR, 0.81; 95% CI, 0.08 to 8.80[5]
	Sedation	4, 667	50	441	7	226	RR, 2.71; 95% CrI, 0.77 to 9.78[2, 4, 5, 7]
	Sedation (12+)	1, 60	3	30	2	30	RR, 1.50; 95% CI, 0.27 to 8.34[36]

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
	Somnolence	6, 1012	119	661	29	351	RR, 2.73; 95% CrI, 1.24 to 7.65[2, 4, 5, 7, 29, 38]
	Somnolence (6to<12)	1, 210	6	146	0	64	RR, 5.75; 95% CI, 0.33 to 100.53[5]
	Somnolence (12+)	1, 146	0	98	0	48	Not estimable[28]
	Hyperprolactinemia	1, 98	1	47	3	51	RR, 0.36; 95% CI, 0.04 to 3.36[4]
	Prolactin-related events	1, 210	1	146	0	64	RR, 1.33; 95% CI, 0.05 to 32.13[5]
	Prolactin-related events (6to<12)	1, 210	3	146	2	64	RR, 0.66; 95% CI, 0.11 to 3.84[5]
Asenapine vs. placebo	Any AE	2, 709	17 132	302 204	4 48	101 102	RR, 1.42; 95% CI, 0.49 to 4.13[8] RR, 1.38; 95% CI, 1.09 to 1.73[9]
	AE limiting treatment	2, 709	17 14	302 204	4 3	101 102	RR, 1.42; 95% CI, 0.49 to 4.13 [8] RR, 2.33; 95% CI, 0.69 to 7.94[9]
	Any EPS	1, 306	16	204	4	102	RR, 2.00; 95% CI, 0.69 to 5.83[9]
	Akathisia	2, 709	5 11	302 204	0 1	101 102	RR, 3.70; 95% CI, 0.21 to 66.39[8] RR, 5.50; 95% CI, 0.72 to 42.01[9]
	Dystonia	1, 403	1	302	0	101	RR, 1.01; 95% CI, 0.04 to 24.60[8]
	Weight (kg)	0					
	BMI ($kg \cdot m^{-2}$)	1, 403	NA	302	NA	101	MD, 0.52; 95% CI, 0.36 to 0.69[8]
	≥7% increase in weight	2, 650	26 19	269 194	1 3	89 98	RR, 8.60; 95% CI, 1.18 to 62.48[8] RR, 3.20; 95% CI, 0.97 to 10.55[9]
	Increased total cholesterol	0					
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	0					
	Increased fasting glucose	0					
	Sedation	1, 306	16	204	2	102	RR, 4.00; 95% CI, 0.94 to 17.06[9]
	Somnolence	1, 306	38	204	7	102	RR, 2.71; 95% CI, 1.26 to 5.86[9]
	Hyperprolactinemia	1, 306	42	204	13	102	RR, 1.62; 95% CI, 0.91 to 2.87[9]
	Prolactin-related events	0					
Olanzapine vs. placebo	Any AE	1, 11	6	6	5	5	RR, 1.00; 95% CI, 0.73 to 1.37[10]
	AE limiting treatment	1, 161	3	107	1	54	RR, 1.51; 95% CI, 0.16 to 14.21[30]
	AE limiting treatment (12+)	1, 60	1	31	1	29	RR, 0.94; 95% CI, 0.06 to 14.27[37]
	Any EPS	0					
	Akathisia	2, 259	3 2	101 72	1 2	51 35	RR, 1.51; 95% CI, 0.16 to 14.20[30] RR, 0.49; 95% CI, 0.07 to 3.31[42]
	Dystonia	0					

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
	Weight (kg)	4, 337	NA	215	NA	122	MD, 3.96; 95% CI, 2.31 to 6.34[10, 30, 37, 42]
	Weight (kg) (12+)	1, 59	NA	30	NA	29	MD, 8.49; 95% CI, 4.90 to 12.08[37]
	BMI ($kg \cdot m^{-2}$)	2, 267	NA NA	107 72	NA NA	54 34	MD, 1.16; 95% CI, 0.93 to 1.39[30] MD, 1.50; 95% CI, 1.06 to 1.94[42]
	≥7% increase in weight	4, 337	99	215	8	122	RR, 6.08; 95% CrI, 1.84 to 27.06[10, 30, 37, 42]
	Increased total cholesterol	1, 109	1	75	0	34	RR, 1.38; 95% CI, 0.06 to 33.07[30]
	Increased LDL	1, 76	0	50	0	26	Not estimable[30]
	Decreased HDL	1, 83	6	51	5	32	RR, 0.75; 95% CI, 0.25 to 2.27[30]
	Increased triglycerides	2, 202	5 20	65 72	0 6	30 35	RR, 5.17; 95% CI, 0.29 to 90.53[30] RR, 1.62; 95% CI, 0.72 to 3.67[42]
	Increased fasting glucose	1, 120	1	81	0	39	RR, 1.46; 95% CI, 0.06 to 35.13[30]
	Sedation	3, 138	16	88	3	50	RR, 2.93; 95% CrI, 0.62 to 14.41[10, 42, 50]
	Somnolence	2, 167	16 12	72 31	1 5	35 29	RR, 7.78; 95% CI, 1.07 to 56.30[42] RR, 2.25; 95% CI, 0.90 to 5.59[37]
	Hyperprolactinemia	2, 268	50 58	107 72	1 6	54 35	RR, 25.53; 95% CI, 3.58 to 177.76[30] RR, 4.70; 95% CI, 2.25 to 9.82[42]
	Prolactin-related events	0					
Paliperidone vs. placebo	Any AE	1, 200	90	149	30	51	RR, 1.03; 95% CI, 0.79 to 1.34[11]
	AE limiting treatment	1, 200	3	149	0	51	RR, 2.43; 95% CI, 0.13 to 46.19 [11]
	Any EPS	0					
	Akathisia	1, 201	14	150	0	51	RR, 9.99; 95% CI, 0.61 to 164.48[11]
	Dystonia	1, 201	6	150	0	51	RR, 4.48; 95% CI, 0.26 to 78.10[11]
	Weight (kg)	1, 200	NA	149	NA	51	MD, 0.90; 95% CI, 0.34 to 1.46[11]
	BMI ($kg \cdot m^{-2}$)	0					
	≥7% increase in weight	1, 200	15	149	1	51	RR, 5.13; 95% CI, 0.70 to 37.90[11]
	Increased total cholesterol	0					
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	0					
	Increased fasting glucose	0					

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
	Sedation	0					
	Somnolence	1, 201	18	150	1	51	RR, 6.12; 95% CI, 0.84 to 44.70[11]
	Hyperprolactinemia	0					
	Prolactin-related events	1, 200	3	149	0	51	RR, 2.43; 95% CI, 0.13 to 46.19[11]
Quetiapine vs. placebo	Any AE	2, 414	68 112	92 147	66 45	100 75	RR, 1.12; 95% CI, 0.93 to 1.35[12] RR, 1.27; 95% CI, 1.03 to 1.56[13]
	AE limiting treatment	5, 748 1, 30	38	458	19	290	RR, 1.21; 95% CrI, 0.30 to 4.73[12, 13, 39, 40, 43] Not estimable[32]
	Any EPS	3, 537	0 7 19	17 193 147	0 1 4	15 90 75	Not estimable[40] RR, 3.26; 95% CI, 0.41 to 26.14 [39] RR, 2.42; 95% CI, 0.86 to 6.87[13]
	Akathisia	1, 19	1	9	0	10	RR, 3.30; 95% CI, 0.15 to 72.08[43]
	Dystonia	0					
	Weight (kg)	6, 778	NA	473	NA	305	MD, 1.44; 95% CI, 0.60 to 2.31[12, 13, 32, 39, 40, 43]
	BMI ($kg \cdot m^{-2}$)	1, 32	NA	17	NA	15	MD, 0.60; 95% CI, 0.39 to 0.81[40]
	≥7% increase in weight	3, 697	70	432	11	265	RR, 3.41; 95% CrI, 0.95 to 18.37[12, 13, 39]
	Increased total cholesterol	2, 185	2 30	17 109	0 2	15 44	RR, 4.44; 95% CI, 0.23 to 85.83[40] RR, 6.06; 95% CI, 1.51 to 24.26[39]
	Increased LDL	2, 286	2 1	17 175	0 0	15 79	RR, 4.44; 95% CI, 0.23 to 85.83[40] RR, 1.36; 95% CI, 0.06 to 33.11[39]
	Decreased HDL	2, 247	3 15	17 154	2 4	15 61	RR, 1.32; 95% CI, 0.25 to 6.88[40] RR, 1.49; 95% CI, 0.51 to 4.30[39]
	Increased triglycerides	3, 463	39	313	9	150	RR, 2.11; 95% CrI, 0.55 to 12.79[13, 39, 40]
	Increased fasting glucose	2, 280	0 2	17 167	1 0	15 81	RR, 0.30; 95% CI, 0.01 to 6.77[40] RR, 2.44; 95% CI, 0.12 to 50.25[39]
	Sedation	6, 778	90	473	32	305	RR, 1.67; 95% CrI, 0.77 to 3.87[12, 13, 32, 39, 40, 43]
	Somnolence	3, 697	106	432	18	265	RR, 2.95; 95% CrI, 0.92 to 8.62[12, 13, 39]
	Hyperprolactinemia	3, 535	33	355	12	180	Value[13, 32, 39]
	Prolactin-related events	0					
Risperidone vs. placebo	Any AE	10, 796	384	443	244	353	RR, 1.25; 95% CrI, 1.13 to 1.40[14-23]
	Any AE (6to<12)	1, 335	82	172	59	163	RR, 1.32; 95% CI, 1.02 to 1.70[34]
	Any AE (12+)	1, 87	10	43	13	44	RR, 0.79; 95% CI, 0.39 to 1.60[27]
	AE limiting treatment	6, 559 3, 239	25	325	7	234	RR, 1.97; 95% CrI, 0.71 to 5.92[14, 17, 19, 21, 23, 31] Not estimable[15, 18, 33]
	AE limiting treatment (6to<12)	2, 374	2 0	172 19	1 0	163 20	RR, 1.90; 95% CI, 0.17 to 20.70[34] Not estimable[35]

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
	Any EPS	5, 636	52	365	13	271	RR, 2.78; 95% CrI, 1.27 to 6.50[14, 18, 20, 21, 23]
	Any EPS (6to<12)	1, 335	3	172	1	163	RR, 2.84; 95% CI, 0.30 to 27.06[34]
	Akathisia	4, 428	39	264	25	164	RR, 1.03; 95% CrI, 0.35 to 4.98[16, 19, 21, 23]
	Akathisia (6to<12)	1, 335	0	172	0	163	Not estimable[34]
	Dystonia	4, 194	0 0 0 0	52 19 10 11	0 0 0 0	63 17 10 12	Not estimable[14] Not estimable[16] Not estimable[17] Not estimable[44]
	Dystonia (6to<12)	2, 358	2 0	172 11	1 0	163 12	RR, 1.90; 95% CI, 0.17 to 20.70[34] Not estimable[44]
	Weight (kg)	14, 929	NA	522	NA	475	MD, 1.52; 95% CI, 0.78 to 2.29[14-22, 33, 45-48]
	Weight (kg) (6to<12)	4, 467	NA	239	NA	228	MD, 2.86; 95% CrI, -1.22 to 7.42[34, 35, 44, 51]
	BMI ($kg \cdot m^{-2}$)	6, 730	NA	397	NA	333	MD, 0.68; 95% CI, 0.27 to 1.18[15, 18, 19, 21, 34, 48]
	BMI ($kg \cdot m^{-2}$) (6to<12)	2, 405	NA NA	172 37	NA NA	163 33	MD, 0.70; 95% CI, 0.49 to 0.91[34] MD, 1.80; 95% CI, -0.61 to 4.21[51]
	≥7% increase in weight	2, 182	13 2	111 6	3 0	58 7	RR, 2.26; 95% CI, 0.67 to 7.63[21] RR, 5.71; 95% CI, 0.33 to 99.97[22]
	≥7% increase in weight (6to<12)	1, 62	29	37	6	33	RR, 4.31; 95% CI, 2.05 to 9.06[51]
	Increased total cholesterol	0					
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	1, 153	1	73	0	80	RR, 3.28; 95% CI, 0.14 to 79.36[46]
	Increased fasting glucose	1, 153	0	73	1	80	RR, 0.36; 95% CI, 0.02 to 8.82[46]
	Sedation	4, 408	52	225	24	183	RR, 2.58; 95% CrI, 0.70 to 14.89[17, 19, 21, 46]
	Sedation (6to<12)	1, 23	5	11	4	12	RR, 1.36; 95% CI, 0.49 to 3.82[44]
	Somnolence	9, 862	163	473	43	389	RR, 3.25; 95% CrI, 1.96 to 5.94[14-16, 18, 19, 33 20, 21, 23]
	Somnolence (6to<12)	1, 335	3	172	2	163	RR, 1.42; 95% CI, 0.24 to 8.40[34]
	Hyperprolactinemia	2, 251	4 6	68 53	4 0	73 57	RR, 1.07; 95% CI, 0.28 to 4.12[46] RR, 13.96; 95% CI, 0.81 to 241.98[18]
	Prolactin-related events	3, 345 5, 457	6	195	3	150	RR, 1.21; 95% CrI, 0.19 to 7.69[18, 19, 21] Not estimable[14, 16, 23, 33, 47]
	Prolactin-related events (6to<12)	1, 335	5	172	0	163	RR, 10.43; 95% CI, 0.58 to 187.10[34]
Various SGA's vs.	Any AE	0					
	AE limiting treatment	0					

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
placebo	Any EPS	0					
	Akathisia	0					
	Dystonia	0					
	Weight (kg)	1, 56	NA	32	NA	24	MD, 3.67; 95% CI, 1.92 to 5.42[49]
	BMI ($kg \cdot m^{-2}$)	0					
	≥7% increase in weight	0					
	Increased total cholesterol	1, 56	3	32	0	24	RR, 5.30; 95% CI, 0.29 to 98.06[49]
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	1, 56	1	32	1	24	RR, 0.75; 95% CI, 0.05 to 11.39[49]
	Increased fasting glucose	1, 56	0	32	0	24	Not estimable[49]
	Sedation	0					
	Somnolence	0					
	Hyperprolactinemia	0					
	Prolactin-related events	0					
Ziprasidone vs. placebo	Any AE	3, 548	300	358	114	190	RR, 1.43; 95% CrI, 0.85 to 2.59[24-26]
	AE limiting treatment	3, 548	33	358	14	190	RR, 1.36; 95% CrI, 0.37 to 6.34[24-26]
	Any EPS	1, 283	22	193	1	90	RR, 10.26; 95% CI, 1.40 to 74.93[25]
	Akathisia	3, 548	22	358	4	190	RR, 2.63; 95% CrI, 0.55 to 13.39[24-26]
	Dystonia	1, 237	1	149	0	88	RR, 1.78; 95% CI, 0.07 to 43.23[24]
	Weight (kg)	3, 360	NA	246	NA	114	MD, -0.10; 95% CI, -1.34 to 1.13[24-26]
	BMI ($kg \cdot m^{-2}$)	0					
	≥7% increase in weight	0					
	Increased total cholesterol	0					
	Increased LDL	0					
	Decreased HDL	0					
	Increased triglycerides	0					
	Increased fasting glucose	0					
	Sedation	2, 264	49 11	149 16	5 5	88 11	RR, 5.79; 95% CI, 2.40 to 13.98[24] RR, 1.51; 95% CI, 0.73 to 3.13[26]
	Somnolence	3, 548	76	358	13	190	RR, 2.97; 95% CrI, 0.84 to 9.96[24-26]
	Hyperprolactinemia	2, 265	17	149	2	88	RR, 5.02; 95% CI, 1.19 to 21.22[24]

Comparison (G1 vs. G2)	Outcome	N Studies, N Patients	G1 Events	G1 N	G2 Events	G2 N	Relative Effects
			5	16	0	12	RR, 8.41; 95% CI, 0.51 to 138.82[26]
	Prolactin-related events	1, 28	1	16	0	12	RR, 2.29; 95% CI, 0.10 to 51.85[26]

AE = adverse event; BMI = body mass index; CI = confidence interval; EPS = extrapyramidal symptoms; G1 = group 1; G2 = group 2; HDL = high density lipoprotein; LDL = low density lipoprotein; MD = mean difference; N = number; NA = not applicable; RR = risk ratio; SGA = second generation antipsychotic

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